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Robert D. Larsen and Joseph L. Posch

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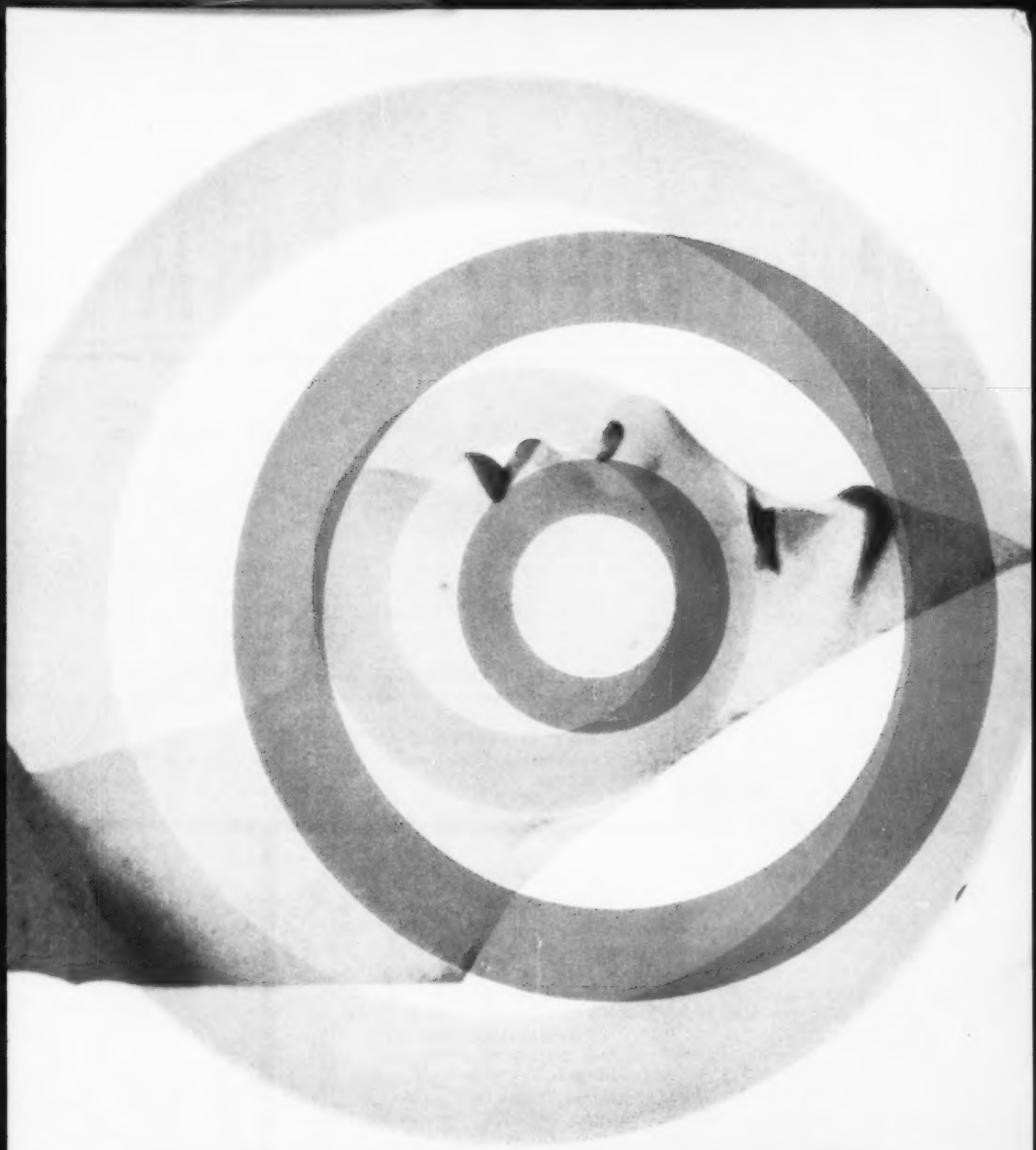

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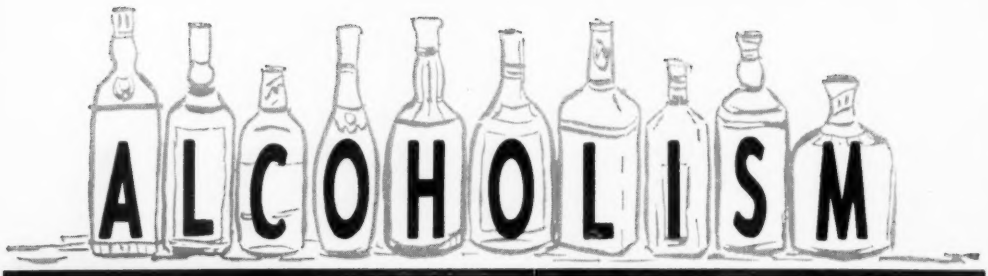

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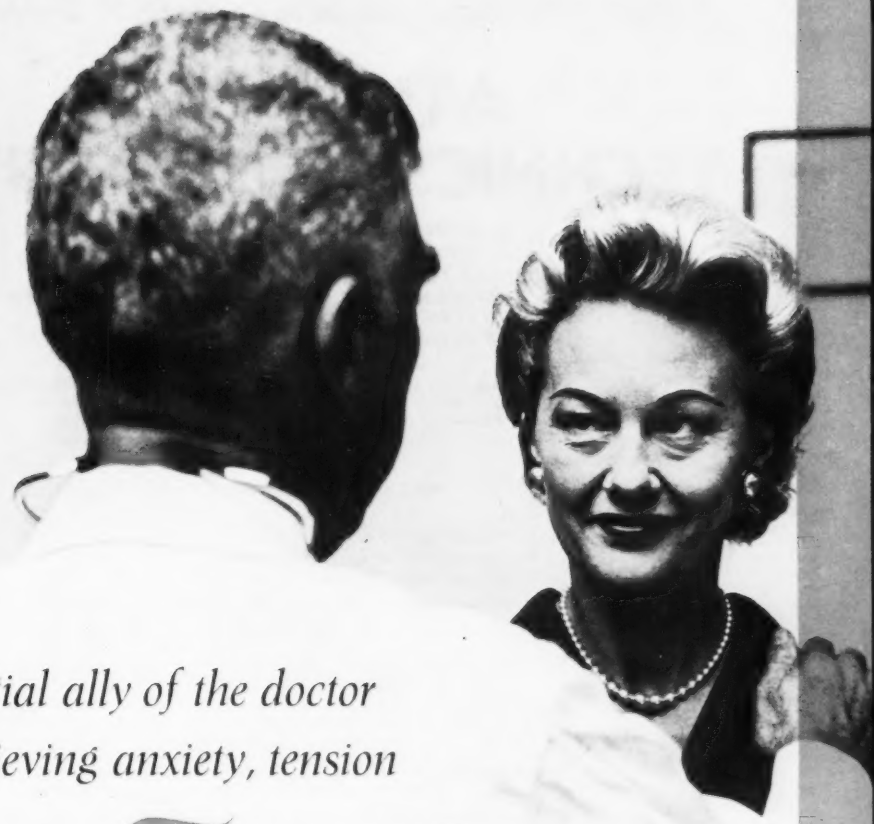

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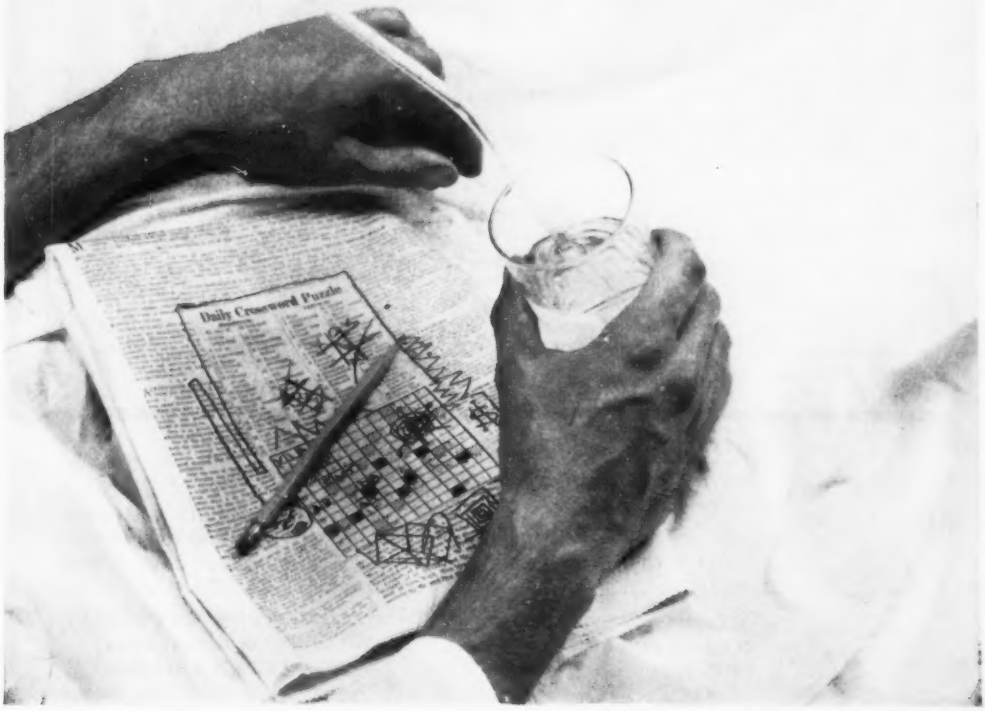

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Nerve Injuries in the Upper Extremity

ROBERT D. LARSEN, M.D., and JOSEPH L. POSCH, M.D., Detroit

The purpose of this paper is to review our experience with the treatment of nerve injuries in the upper extremity. Since 1950 we have had an opportunity to treat 325 cases of this type. Tables 1, 2, and 3 summarize the nerves which were injured and the level of the injury. In those cases in which more than one nerve was injured, as in multiple lacerations of the digits or combined median and ulnar nerve lesions in the wrist, the injury is counted as a single case. This group of patients was treated between January, 1950, and January, 1957. The follow-up period varies from one to seven years.

Age and Sex

One hundred ninety-five of these patients were men and eighty-one women. There is no difference in the results of nerve repair attributed to the patient's sex. Forty-nine of the patients were 14 years of age or younger (Table 4). As in tendon repair and fracture healing, the results of nerve repair in children are superior to the results obtained in adults.

Submitted for publication March 28, 1958.

Read at the 15th Annual Assembly of the Central Surgical Association, Columbus, Ohio, Feb. 20, 1958.

From the Department of Surgery, Wayne State University College of Medicine; the Surgical Service of the Receiving Hospital of the City of Detroit, and the University Service of the Grace Hospital.

TABLE 1.—*Nerves Injured in Hand*

Proper digital—1	93
Proper digital—2	65
Common digital	14
Recurrent median	3
Median (proximal palm)	10
	155

TABLE 2.—*Nerves Injured in Wrist and Forearm*

Median—wrist	42
Median—forearm	6
Ulnar—wrist	36
Ulnar—forearm	9
Ulnar (dorsal sensory)	6
Median and ulnar—wrist	26
Median and ulnar—forearm	1
Radial—motor	5
Radial—sensory	6
	137

Etiology

Fifty-nine of the injuries were sustained while the patient was at work. Two hundred sixty-six were nonindustrial in origin. Those in the latter category were mostly accidental injuries, but a few were wounds of violence and attempted suicides (Table 5). A porcelain faucet injury is illustrated in Figure 1.

TABLE 3.—*Nerves Injured—Arm and Above*

Median	5
Ulnar	6
Radial	17
Median and ulnar	2
Posterior cord plexus	1
Spinal accessory	1
Musculocutaneous plexus	1
	33

TABLE 4.—*Nerve Injuries*

Male (adult)	195
Female (adult)	81
Children	49
Industrial	59
Nonindustrial	266
Associated tendon injury	236
Associated fracture	25

TABLE 5.—*Nerve Injuries—Etiology*

Glass	125
Porcelain faucet	8
Knife	63
Saw	41
Machinery	48
Miscellaneous sharp	24
Miscellaneous crushing	16
	325

Diagnosis

In most cases of nerve injury the level of the injury is clearly indicated by a wound. However, in those injuries which are not accompanied by a surface wound one must rely upon one's knowledge of anatomy to determine the level of the lesion. It is beyond the scope of this paper to review the detailed anatomical descriptions of the upper extremity nerves. These descriptions are found in any standard anatomy text. An excellent discussion of the sensory and motor changes caused by injury to each of the nerves in the upper extremity may be found in Bunnell's text.[5] Figures 2 and 3 illustrate the usual sensory nerve distribution in the upper extremity. Figures 4, 5, and 6 show the clinical tests which are used to examine the motor functions of the ulnar, median, and radial nerves, respectively.

In addition to testing the integrity of the sensory and motor nerves of the extremity, one should look for injured tendons and for fractures. Of the 325 patients, 292 had injuries below the elbow. Of the nerve injuries below the elbow, 236 were accompanied by tendon injuries. Of the 325 patients, 25 had fractures associated with the nerve injury.

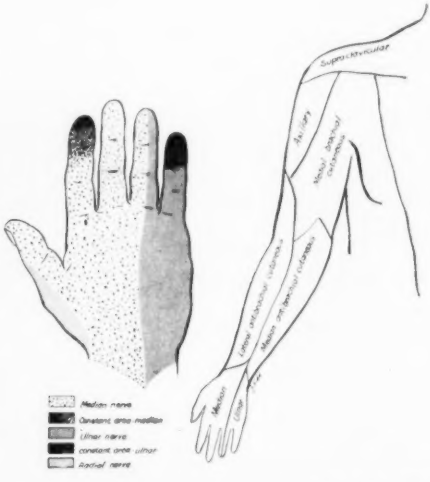
In young children and in uncooperative older children, a diagnosis usually cannot be made by testing for motor function or sensory loss. Here one must rely upon the anatomical relationships of the nerve. If the wound lies over the course of a major nerve, and one cannot conclusively demonstrate that the nerve is intact, it has been our policy to explore the wound under anesthesia.

Operative Technique

The repair of peripheral nerves is a simple but exacting task. Debridement of both

Fig. 1.—Porcelain faucet injury. Structures injured were the flexor pollicis longus tendon and the branches of the median nerve to the thumb and index finger.

Fig. 2.—Distribution of sensory nerves to the anterior surface of the extremity and the volar surface of the hand.



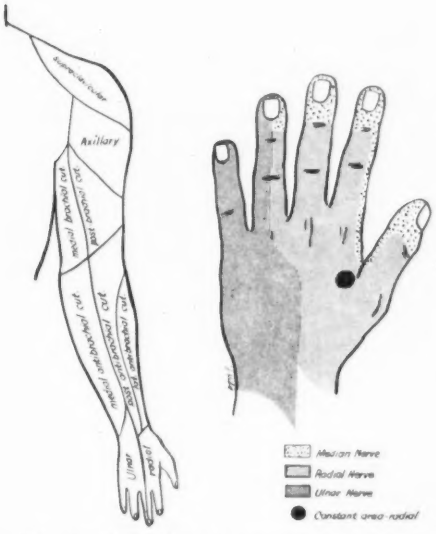


Fig. 3.—Distribution of sensory nerves to the posterior surface of the extremity and the dorsal surface of the hand.

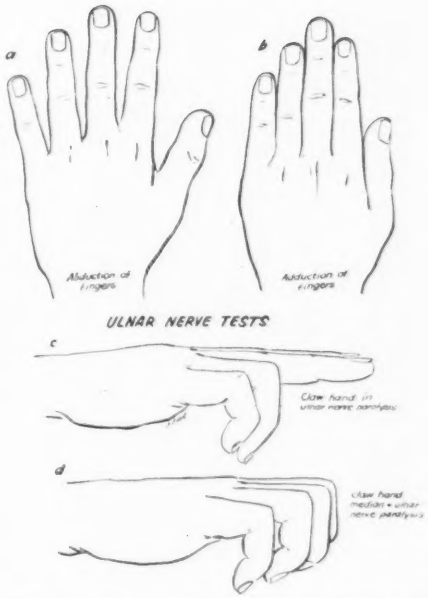


Fig. 4.—(*a* and *b*) Abduction and adduction of the fingers. This motion is lost in ulnar paralysis. (*c*) Claw hand in ulnar paralysis; (*d*) claw hand in combined median and ulnar paralysis.

ends of a severed nerve is necessary. In fresh, cleanly incised wounds only a few millimeters of nerve are removed. In secondary repairs all scar should be excised. If any of the scar, or proximal neuroma, or distal glioma is allowed to remain, success will be jeopardized (Fig. 7).

An accurate end-to-end suture is mandatory. The suture material should be the finest possible. Use of 000000 or 0000000 black silk with a swedged-on needle will be

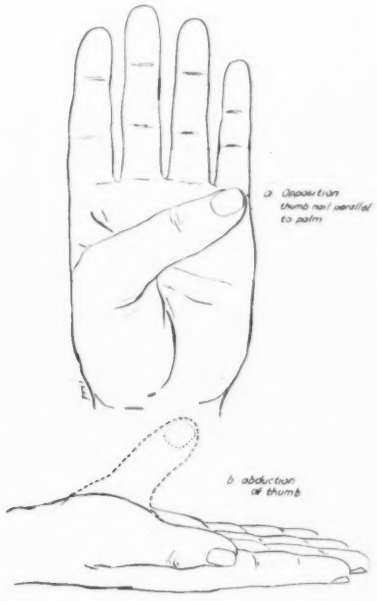


Fig. 5.—Tests to determine function of intrinsic muscles of the thumb which are supplied by the median nerve.

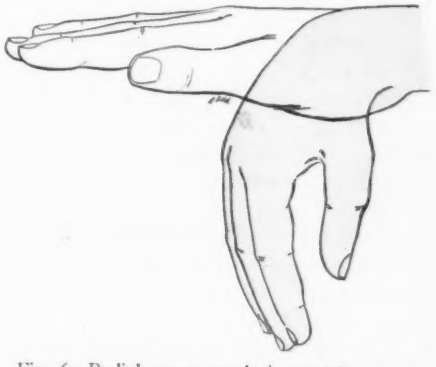


Fig. 6—Radial nerve paralysis resulting in inability to extend the wrist, thumb, and metacarpophalangeal joints of the fingers.

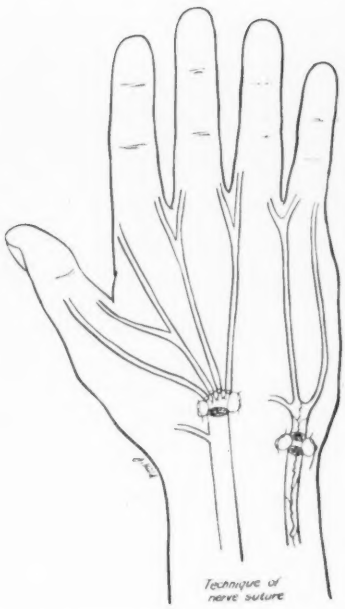


Fig. 7.—Technique of nerve repair when a nerve is divided while it is a single trunk and when it is lacerated at the point of division into its branches.

adequate in most cases. The suture passes only through the nerve sheath with the knots tied outside the nerve, so that as little foreign body as possible is in contact with the nerve fibers. Rotation of the two ends in their relation to each other should be avoided. Often small vessels or prominent bundles of nerve fibers will be noted on the nerve that will help in preserving the proper axial alignment.

Care must be taken to avoid tension on the suture line. Often dissection along a considerable length of each nerve end or transplantation of the nerve will be necessary before suture can be made without tension. In cases in which there is a gap between the nerve ends that cannot be overcome by dissection or by transplantation, repeated mobilization and stretching of the nerve may result in eventual approximation of the nerve ends.

Case 1.—A 23-year-old police officer was shot at close range in the forearm with a high-powered rifle on March 6, 1955. The injury resulted in loss

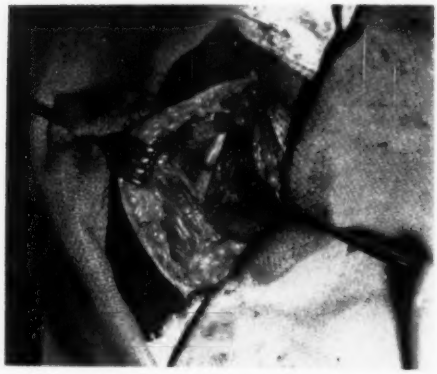


Fig. 8.—Sutured radial nerve in the midarm. Extensor function began to return at six months and was excellent after one year.

of considerable skin and subcutaneous tissue, the midshaft of the radius, 4 in. (10 cm.) of the median nerve, and several flexor and extensor tendons and muscles on the radial side of the forearm.

At each reconstructive operation, one of which was restoration of the radius with a fibular graft (Fig. 9), the two ends of the median nerve were mobilized and advanced toward each other. During the fifth operation (flexor tendon grafting) the median nerve was sutured. The first signs of sensory return were observed six months later. At the time of this report, two years later, sensation is almost normal. There is electromyographic evidence of reinnervation of the thenar muscles, but clinically their function is not impressive.

When the gap between the nerve ends is so large that it cannot be overcome by mobilization of the nerve, nerve graft is necessary. At times one digit may require amputation while an adjacent digit is reconstructed. If the digit to be reconstructed has a large gap between the ends of a sensory nerve, the nerve from the amputated digit may be used as a graft to bridge the defect. If such a convenient donor nerve is not available, the sural nerve is the donor nerve of choice. Several segments of sural nerve may be sutured together to form a cable graft and used to overcome defects in larger nerves.

Bunnell and Boyes [4] have reviewed their clinical and experimental experience with nerve grafts. Our experience with nerve

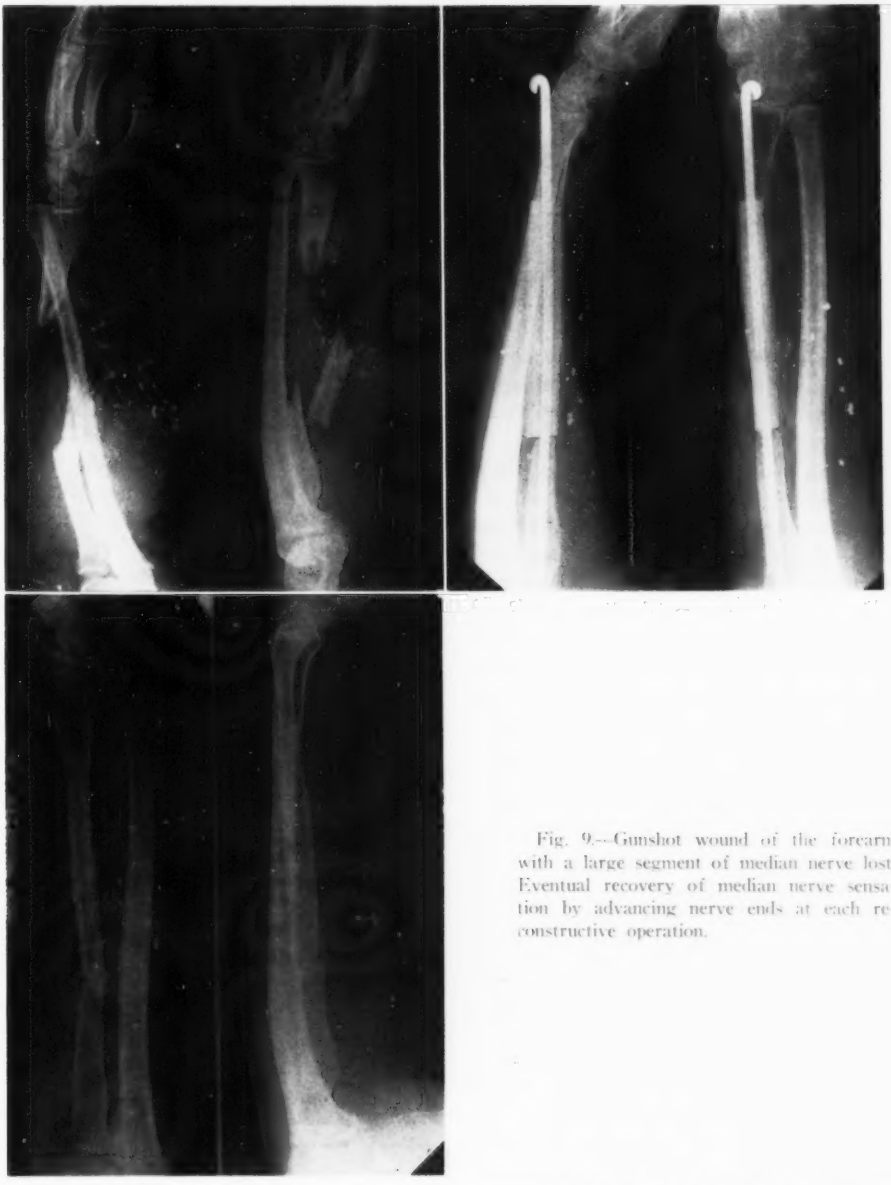


Fig. 9.—Gunshot wound of the forearm with a large segment of median nerve lost. Eventual recovery of median nerve sensation by advancing nerve ends at each reconstructive operation.

grafts is not large. The results in our few cases conform to the experience of Bunnell and Boyes. Nerve graft is a useful operation when the nerve ends cannot be approximated in any other way.

In repair of lacerations of the major nerves, we have used 8 to 10 interrupted sutures of fine black silk. In the common digital nerves in the palm, three or four sutures will be sufficient, while in the digital nerves within the fingers two sutures are enough to provide accurate approximation. We have not used the continuous fine silk suture, fearing that as the nerve swells,

the suture might cause constriction of the nerve.

Primary or Secondary Neurorrhaphy

When conditions permit, we have chosen to repair injured nerves primarily. Given ideal conditions of the wound and ideal operating conditions, the results of primary neurorrhaphy have been somewhat better than the results of secondary neurorrhaphy in our cases. Bunnell [5] and Siler [12] support the primary repair of nerves in ideal wounds. Zachary and Holmes [15] report better results from early secondary repair. Probably the difference lies in the selection of cases for primary suture.

When one finds evidence of a partial laceration of a major nerve, we feel that it is especially important to carry out primary repair. At the time of injury, the injured portion of the nerve is quite obvious, and its accurate repair is easily performed. Secondary repair of a partially lacerated nerve is not as satisfactory. The neuroma and glioma at the point of laceration and the surrounding scar obscure the intact fibers and make their identification most difficult. If the nerve has not been repaired primarily, secondary repair should be carried out as soon after the injury as possible. In general, this means that the secondary repair will be performed about three weeks after the injury. Woodhall [13] feels that all nerves should be sutured within three months of the injury, ideally. If there has been infection of the wound, this must be allowed to subside completely, including absence of redness or edema around the wound, before the nerve repair is performed. Nerves may be repaired any time after the injury; however, the longer one waits, the less likely one is to obtain a good result. Up to 12 to 18 months the return of sensation after nerve repair may be expected to be quite good. After two years the chances of success begin to diminish. One should, however, repair the injured nerve whenever it is found. In one female patient the median nerve at the wrist was repaired 14 years after the injury. The patient obtained partial return of sensation but, of course, no return of the thenar muscles. Muscles which have lost their nerve supply undergo fibrous degeneration quite rapidly, so that early repair of injured motor nerves is essential.

Contraindications to primary nerve repair include severe crushing or tearing, marked contamination of the wound, associated injuries of a higher priority, and inadequate facilities for the operation. Extensively crushed or torn nerves usually have damage extending beyond the point of division of the nerve. Nerve fibers are torn above and below the level of the wound. This cannot be noted grossly at the time of the injury. In such a wound secondary neurorrhaphy is better. Wound infection reduces the success of nerve suture. The nerve itself is quite resistant to infection, but regeneration across the suture line is delayed or prevented by infection. Cleanly incised wounds caused by glass, knives, and other relatively clean instruments rarely become infected. Nerve repair is successful in such a wound. Wounds heavily contaminated by ground-in dirt or by instruments known to be contaminated may become infected. Nerve repair should be done secondarily in such wounds. The absence of adequate operating facilities precludes a good result from peripheral nerve surgery. Peripheral nerve repair is not a procedure to be carried out in an emergency room. The best of operating facilities, including anesthesia and assistants, is needed. Secondary neurorrhaphy is to be preferred if these facilities are not available.

Tinel's sign will aid the evaluation of sensory nerve regeneration. Tapping over the regenerating axons may produce sensations in the distribution of the nerve before any other evidence of regeneration is detectable. Electromyography will supply information about the state of paralyzed muscles which cannot be obtained in any other way. Electromyographic evidence of reinnervation of muscles can be obtained be-

fore there is any clinical sign of regeneration. Too great a reliance should not be placed upon the electromyogram, however. The exploring electrode may encounter isolated areas in the muscle which show a pattern of nerve regeneration while the major portion of the muscle is not being satisfactorily reinnervated. Conversely, the electromyogram may show a pattern of denervation fibrillation at the same time that voluntary contraction of the muscle can be palpated. The electromyographic studies must be correlated with the clinical observations.

Care After Nerve Repair

A large compression dressing is applied after the operation. Compression is supplied by elastic bandages, which are loosened the following day. The extremity is splinted with either plaster or aluminum splints, so that the suture line in the nerve is relaxed. Median and ulnar nerve repairs at the wrist are protected by a posterior splint which holds the wrist in flexion. About 10 to 15 degrees less than full flexion is used. A wrist forced into maximum flexion and immobilized there will be stiff for several months postoperatively, and is usually painful during the immobilization. We have not found it necessary to splint the elbow in nerve repairs about the wrist, but the patient wears a sling whenever ambulatory. Repairs between the midarm and the midforearm require splinting of the elbow. Nerve repairs above the midarm require immobilization of the shoulder. Nerves sutured in the digits may be splinted with the hand in the position of function unless wrist flexion is needed to protect a sutured tendon or tendon graft.

The sutured nerve should be protected by continuous splinting for four weeks. After this, gradual motion of the immobilized joint can be allowed. In the wrist, the splint can be removed entirely at the end of four weeks. There will be enough stiffness of the wrist to act as a natural splint for several more weeks. In the elbow and shoulder the nerve should be gradually stretched by changing the angulation of the splint for the fifth and sixth weeks. The elbow and shoulder recover motion more rapidly after splinting than the wrist, so that additional protection is needed.

Splinting for protection of paralyzed muscles and for the prevention of contractures is sometimes necessary while awaiting regeneration of the nerve. Median nerve injuries seldom require splinting of the paralyzed muscles. In median nerve lesions above the branches to the long flexor muscles, there is loss of flexion of the distal joint of the thumb and the distal two joints of the index and middle fingers. These joints should be passively exercised several times a day, but splinting usually is not necessary. Splinting of the thumb for thenar muscle paralysis is unnecessary, since very little joint stiffness results from this lesion.

Patients vary greatly in their response to ulnar nerve paralysis. Some rapidly develop severe clawing of the ring and little fingers; others show no clawing at all, in spite of obvious interosseous muscle atrophy. Flexion contractures of the interphalangeal joints frequently develop after the ring and little fingers have been clawed for a few weeks. This deformity is easier to prevent than it is to correct. Established interphalangeal joint contractures are very difficult to correct, and they limit the results obtained from tendon transfer operations. Patients who show that they are going to develop a severe degree of clawing require early splinting. Hyperextension of the metacarpophalangeal joint should be prevented. This can be accomplished by a leather strap placed across the dorsum of the proximal phalanges and pulled toward the wrist by a rubber band, as illustrated by Littler.[11] If joint contracture has already started, it can be arrested or overcome by use of the miniature reverse knuckle-bender splints, designed by Bunnell, and made by H. Weniger Co., of San Francisco (Fig. 10).

Radial nerve paralysis requires continual splinting of the extensors of the wrist, thumb, and fingers until the paralysis is

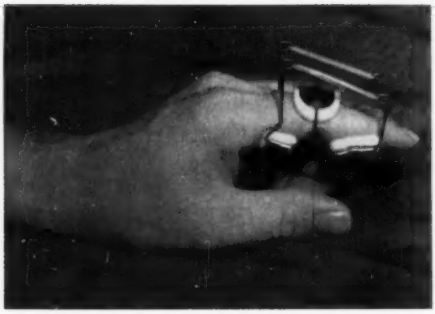


Fig. 10.—Reverse knuckle-bender splint designed to overcome flexion deformities of the proximal interphalangeal joint.

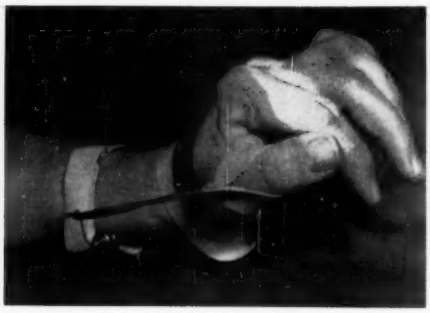


Fig. 11.—Oppenheimer splint for radial nerve paralysis. This simple apparatus is very effective in protecting the paralyzed muscles until reinnervation occurs.

overcome. We have found the Oppenheimer splint to be the most satisfactory for this purpose (Fig. 11). Patients have worn this splint day and night for many months without difficulty.

We have not routinely used electrical stimulation of paralyzed muscles in the postoperative period. Stimulation of the muscles six days a week until recovery occurs is not ordinarily practical in private practice. Those of our patients who did receive electrical stimulation were treated two or three times a week. No benefit could be detected on this reduced schedule.

Results of Nerve Repair

The rate of nerve regeneration following repair is said to be about 1 to 4.5 mm. a day.[1] The latter figure seems higher than the usual rate encountered clinically. Paresthesias, numbness, tingling, and various bizarre sensations usually appear before the return of true sensation. The paresthesias are followed by hyperesthesia, which may become very troublesome. The hyperesthesia gradually subsides, and relatively normal sensation appears. Two-point tactile discrimination is the sensation which most frequently fails to return to normal. Normally, on the tactile pads of the fingers two points can be distinguished when they are 2.3 mm. apart.[2]

It has been stated that the digital branches of the median and ulnar nerves are so small that suturing them is out of the question.[10] We disagree with this point of view and suture digital nerves as far distal as the distal interphalangeal joint. The return of sensation following suture of various nerves is indicated in Table 7.

Six patients required nerve graft (Table 6). Four grafts were obtained from amputated digits and transferred to digits being reconstructed. Two grafts were from the sural nerve. In one case a 2.5 in. (6.5 cm.) defect in a digital nerve was bridged. In the other the sensory branches of the median

TABLE 6.—*Operation Performed*

Primary repair	177
Secondary repair	135
Nerve graft	6
No surgery	7
	325

TABLE 7.—*Return of Sensation Following Nerve Suture*

Level of Nerve Injury	Group *		
	1	2	3
Digital (142)	92	41	9
Median (wrist and palm) (78)	56	20	2
Median (arm and forearm) (14)	6	7	1
Ulnar (wrist) (62)	39	20	3
Ulnar (forearm and arm) (18)	8	8	2
Radial (arm) (17)	10	6	1
Radial (senory) (6)	5	1	0

* Group 1: Can distinguish sharp from dull, hot and cold, coarse and light touch and two points 1 cm. or less apart.
Group 2: Can distinguish the same sensation as Group 1 except that two-point tactile sensation is poor or absent.
Group 3: Can distinguish pain and coarse touch only.

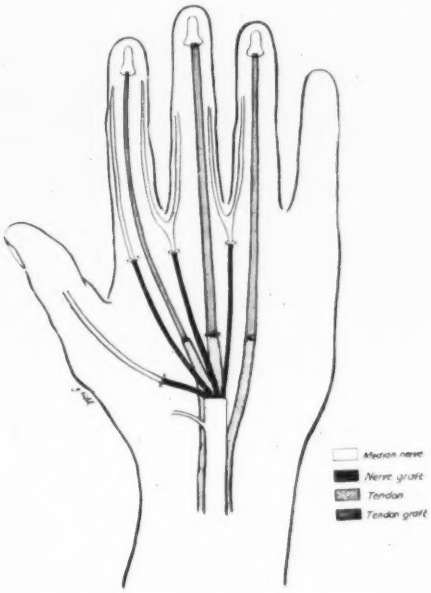


Fig. 12.—Tendon grafts and nerve grafts from the sural nerve after the tendons and nerves had been destroyed by hot plastic injected into the palm under pressure.

nerve to the index, middle, and ring fingers had been destroyed when hot plastic, under pressure, was accidentally injected into the palm. After successful pedicle grafting of the palm, simultaneous tendon and nerve grafts were placed in the palm. This procedure is detailed in Figure 12. In the five cases of nerve graft to the digital nerves good return of sensation was achieved. In the case of multiple grafts satisfactory sensory return as far as the middle finger segments was obtained. Diminished sensation

TABLE 8.—*Results of Median Nerve Repair*

	Yes	Partial	No
Proximal palm and wrist (78)			
Thenar muscle return (54 primary repairs)	35	0	19
Thenar muscle return (24 secondary repairs)	12	0	12
Arm and forearm (14)			
Thenar muscle return	5	2	7
Arm (7)			
Long flexor return	6	1	0

TABLE 9.—*Results of Ulnar Nerve Repair*

	Yes	Partial	No
Wrist (62)			
Intrinsic muscle return	0	23	39
Arm and forearm (18)			
Intrinsic muscle return	0	0	18
Arm (8)			
Long flexor return	6	2	0

at the finger tips was still present two years after surgery.

The return of voluntary motor function following suture of the median, ulnar, and radial nerves is indicated in Tables 8, 9, and 10, respectively. Two-thirds of the 54

TABLE 10.—*Results of Radial Nerve Repair*

	Yes	Partial	No
Below elbow (5)			
Extensor return	1	1	3
Above elbow (17)			
Extensor return	13	1	3

Fig. 13.—Return of opposition and abduction of the thumb one year after primary repair of a completely divided median nerve at the wrist.

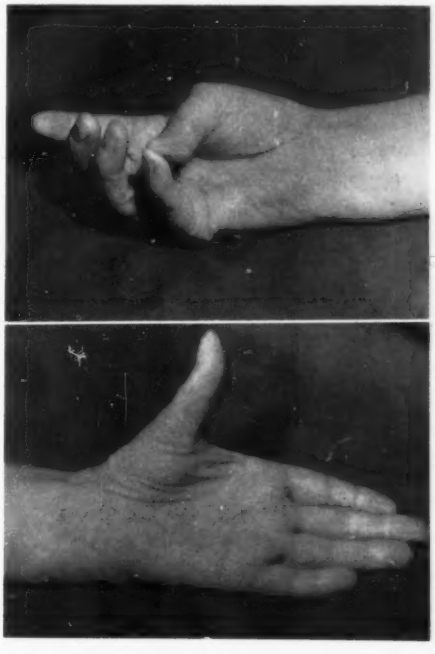


Fig. 14.—*A*, return of flexor digitorum profundus innervation six months after primary repair of the ulnar nerve at the elbow. Note flexion of the distal phalanges of the ring and little fingers. *B*, same patient. Note the lack of clawing in spite of complete atrophy of the interosseous muscles.

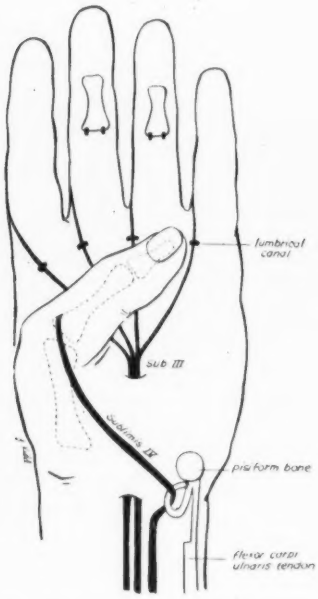


Fig. 16.—Schematic drawing of opponens transfer for thenar muscle paralysis, using the sublimis tendon from the ring finger as the motor tendon, and schematic drawing illustrating the essential features of sublimis tendon transfer for interosseous and lumbrical muscle paralysis.

patients who had primary repair of the median nerve in the proximal part of the palm or wrist regained the function of the thenar muscles (Fig. 13). One-half of the secondary median nerve neurorrhaphies at this level regained thenar muscle function. Return of function of the long flexors after repair of the median nerve in the arm is usual.

Complete return of the function of the intrinsic muscles of the hand after ulnar nerve suture was not observed. Return of long flexor function after ulnar nerve repair in the arm was usual (Fig. 14*A* and *B*).

Fig. 15.—Return of extension of the wrist and partial return of finger extension one year after primary repair of the radial nerve in the upper arm. The patient is still improving.

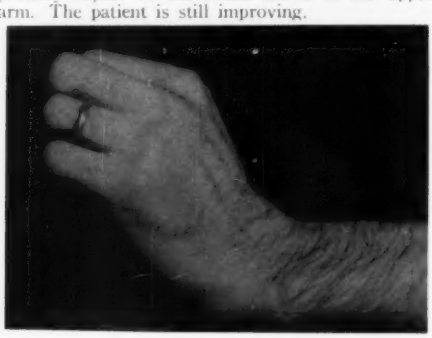


Fig. 17.—Ability of a patient with thenar muscle paralysis to oppose the thumb to the little finger after transfer of the ring finger sublimis tendon to the thumb. Note that pulp-to-pulp pinch is absent.

Fig. 18.—Claw hand following combined median and ulnar nerve laceration at the wrist. This case was treated as outlined in Figure 16, with sublimis tendon transfer to the lateral bands. (*A*) Maximum preoperative finger extension; (*B*) postoperative extension; (*C*) postoperative flexion.

Radial nerve repair above the elbow resulted in return of extension in the wrist, fingers, and thumb in 13 of 17 cases (Fig. 15). Radial nerve repair below the elbow (where the nerve rapidly divides into several branches) was not as satisfactory.

Tendon Transfers and Other Reconstructive Operations

When motor function has failed to return after nerve repair, various reconstructive operations are indicated. Almost all of these operations are directed toward restoration

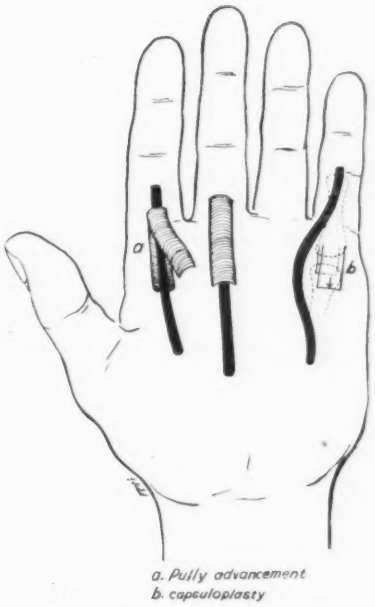


Fig. 19.—Two simple operations to correct clawing of the fingers in intrinsic muscle paralysis. (*a*) The pulley advancement operation; (*b*) capsuloplasty of the metacarpophalangeal joint.

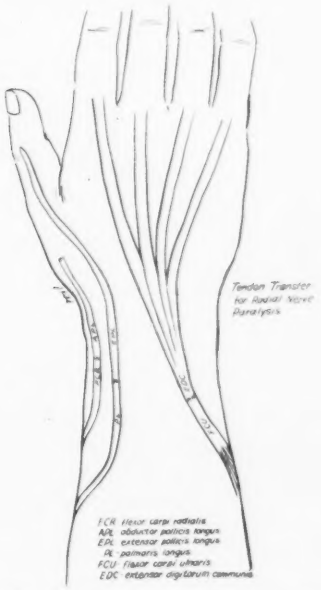

Tendon Transfer for Radial Nerve Paralysis
FCR: flexor carpi radialis
ABL: abductor pollicis longus
EPL: extensor pollicis longus
PL: palmaris longus
FCU: flexor carpi ulnaris
EDC: extensor digitorum communis

Fig. 20.—Schematic drawing illustrating one method of tendon transfer for paralysis of the radial nerve.

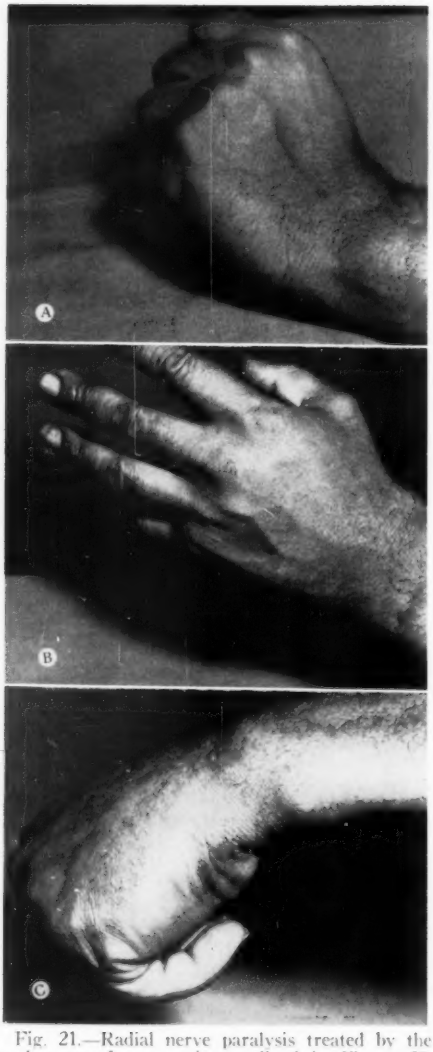


Fig. 21.—Radial nerve paralysis treated by the tendon transfer operation outlined in Figure 20. (*A*) Postoperative wrist extension; (*B*) postoperative finger extension; (*C*) postoperative wrist flexion.

of motion in the hand and in the wrist. It is impossible to discuss all of these procedures in a single paper. A brief résumé of those we have employed most often follows.

Opponens transfer for thenar muscle paralysis is usually performed by transferring the flexor digitorum sublimis tendon of the ring finger to the proximal phalanx of the thumb, as illustrated in Figure 16. Satisfactory opposition is obtained, but pulp-to-pulp pinch is seldom restored (Fig. 17). This procedure is thoroughly discussed by Bunnell.[6] Variations of this operation are described by Littler[11] and by Flynn.[9]

Claw hand following ulnar or median and ulnar nerve paralysis can occasionally be corrected by such simple operations as pulley advancement (Fig. 19*A*) or the capsuloplasty of Zancolli[16] (Fig. 19*B*). Usually, however, transfer of the sublimis tendons through the lumbrical canals to the lateral bands is required (Fig. 16). This procedure has seemed to us to give the best results (Fig. 18*A*, *B*, and *C*).

Permanent radial nerve paralysis can be corrected by one of many tendon transfer operations. One such procedure is illustrated in Figure 20. The postoperative function of a patient with complete radial paralysis is shown in Figure 21*A*, *B*, and *C*. Usually joint stiffness or contracture is not a problem in radial nerve paralysis, even though the paralysis may have existed for a number of years.[3] Bunnell[7] has discussed the various types of tendon transfer for radial paralysis and the technical details which must be observed if good results are to be obtained.

Summary and Conclusions

1. Nerve injuries in the upper extremity are among the more important means of partially or completely crippling the extremity.

2. Accurate anatomical knowledge is necessary in order properly to diagnose and treat a nerve injury in the upper extremity.

3. Immediate or primary repair of the nerve is favored whenever possible.

4. In cases of contaminated, crushed, or torn wounds, or when adequate operating facilities are not available, secondary repair is to be preferred.

5. Sensory return, after nerve repair, is uniformly good. Except in children, there is almost always some sensory deficit demonstrable by careful testing.

6. Return of motor function following nerve suture is most satisfactory in the radial nerve and is satisfactory in one-half to two-thirds of the cases in the median nerve at the wrist. Motor return is uniformly unsatisfactory in ulnar nerve lacerations, regardless of where they are encountered.

7. Tendon transfer operations are available to restore function to a permanently paralyzed portion of the extremity. These procedures are briefly described.

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DISCUSSION

DR. VINTON E. SILER, Cincinnati: Dr. Larsen and Dr. Posch have given us an excellent discussion of a difficult problem and have covered a large amount of material in their 10-minute period. I had an opportunity to read their paper last night, having received it yesterday, and I believe all of you will enjoy reading the published manuscript.

I noted that in the 325 cases Dr. Larsen presented 292 injuries occurred below the elbow. Of these 292 nerve injury cases, 236, or 80%, were combined with tendon injury. I think this combination is the crux of the problem, for associated nerve and tendon injuries indicate the surgical skill necessary to convert this type of injury to a good functional result.

Last year we reported 107 cases of combined nerve and tendon injury, and I should like to tell you something about the results.

(Slide) In the hand, particularly, we pointed out that injuries occurring within the tendon sheath, from its origin in the palm to the distal end, were considered as lying in Zone 1. Injuries from the distal edge of the transverse volar ligament to the origin of the tendon sheath we considered as occurring in Zone 2, and any injury occurring proximal to the distal edge of the volar ligament we considered as in Zone 3.

This drawing gives some idea of the nature of the complexity of the ulnar and median nerve in this region. I would like to point out particularly the branching of both these nerves distal to the transverse volar ligament. This area is one in which repair of nerve damage is most difficult, and in our experience has given very poor results.

(Slide) I would like to emphasize some of the principles which Dr. Larsen could not discuss because of the time factor. First of all, the correct anatomical diagnosis is important. This can be made in the majority of cases, with the exception of some children and, in particular, the drunken patient. This implies that one must attend to detail. The surgeon must have interest in hand injury, and if he uses anatomical knowledge he should be able to make a correct diagnosis.

Second, the proper application of the pneumatic tourniquet is most important. I would like to repeat that the narrow cuff is dangerous and should not be used in the upper extremity; this is true regardless of statements made to the contrary. In addition, I think that any use of the tourniquet beyond the two-hour period is going into a dangerous length of time, although we have used it for as long as four hours provided there

is no air leak in the pneumatic system. The pressure should range around 260 mm. Hg.

Third, one has to plan one's surgical approach. I would agree entirely that primary neurorrhaphy is superior to secondary or delayed neurorrhaphy when the indications are present.

Finally, the application of intelligent splinting is most important, and, in addition, the value of directed physical therapy in the recovery period cannot be minimized.

(Slide) This slide shows the results for the 107 cases we have followed. We did not study any case we could not follow more than two years; hence, we had only 89 patients for study. In this group, as you will see by the zones indicated, the over-all good results were 82%.

Again, I repeat that this paper by Dr. Larsen and Dr. Posch has been most interesting and enlightening, and I am sure all of you will enjoy reading the entire paper.

Dr. Edward Mason, Iowa City: I noticed that Dr. Larsen had only one case of musculocutaneous nerve injury, and I would like to ask him and Dr. Siler for a prognosis with regard to a patient whose slide we shall now see.

(Slide) This Iowa farmer was chasing a chicken thief, a cat, and he fell on the butt of his gun. He blew a hole in his shoulder. He had failure of extension of the wrist, inability to flex the forearm and upper arm, paralysis of the deltoid muscle, and no pulse.

We found that he had blown out about 3 cm. of his axillary artery and the musculocutaneous nerve, had taken a nick out of the axillary nerve, and had contused the posterior cord. The posterior cord and radial nerve were intact, and the vein was intact.

We trimmed off about 1 cm. at each end of the axillary artery and put in this graft. We then took the medial antibrachial cutaneous nerve, as much of it as we could, cut it in two, and put the two pieces side by side, making a cable graft, as you can see here, for the musculocutaneous nerve. We saw the patient nine hours after the initial injury. His pulse has been excellent. It has been six weeks since his injury, and we know nothing about what the final results will be.

Dr. Robert D. Larsen, Detroit: Dr. Siler brought up the point in the written manuscript concerning diagnosis in children. I would say briefly that when we cannot demonstrate conclusively that the nerve is intact, our policy is to explore.

With regard to the case illustrated, that of the gunshot wound in the musculocutaneous nerve and axillary artery, our one musculocutaneous nerve injury was a simple laceration, a direct stab wound, and that patient had good biceps function about eight months after primary neurorrhaphy.

Malrotation of the Midgut in Infancy and Childhood

WILLIAM B. KIESEWETTER, M.D., and JOHN W. SMITH, M.D., Pittsburgh

Most physicians who encounter the entity which is the subject of this paper term it "malrotation of the colon." It could, perhaps, be more correctly entitled "malrotation of the midgut," since it is not always a failure of the rotational process of the colon that produces the symptomatology. In fact, one of the early descriptions of this condition is found in the medical literature of the late 18th century, when Neubauer [1] described paraduodenal hernia. Again, Reid, in 1836, and Simpson, in 1839,[1] described some of the rotational anomalies that occur as a basis for the symptomatic cases. Eventually, in 1904, Mohring [1] reported the first successful surgical treatment of a midgut volvulus that was caused by a rotational abnormality.

Our interest has been drawn to this pathological condition by having seen five such cases in the past 12 months at the Children's Hospital of Pittsburgh. We reviewed the hospital experience in this condition from 1940 to 1957 and found that 44 cases had come to operation during this period. There were also six autopsy cases in which death was from other causes and in which the finding of a malrotation was incidental. A review of the embryology of the midgut and an analysis of the experience in these cases forms the basis of this paper.

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Embryology

Many of the conditions which one runs into in pediatric surgery find a ready etiologic explanation when one surveys the embryonic development of the area involved. This is particularly true of aberrations of the rotational process of the midgut.

By "midgut" the embryologist refers to that portion of the intestinal tract that is supplied by the superior mesenteric artery. It begins at the second portion of the duodenum and extends through the small intestine to a point in the midtransverse colon. The midgut is further divided into prearterial (jejunum and upper ileum) and postarterial segments (lower ileum and ascending colon), the main branch of the superior mesenteric artery being used as the point of reference.

Frazer and Robbins [2] very ably described the embryology of the midgut, and they divided it into three stages.

Stage I (up to the tenth week).—The midgut normally resides in the umbilical cord during the first 10 weeks of gestation because the abdominal cavity cannot hold the enlarging liver and growing intestine. An 180 degree counterclockwise rotation occurs late in this stage to place the postarterial segment anteriorly and the prearterial posteriorly.

Anomaly of Stage I: Failure of the rotational process to go beyond the first stage, with retention of the midgut in the umbilical stalk, results in the newborn condition known as *omphalocele*.

Stage II (ten to eleven weeks).—This is the time interval during which the midgut retracts from the umbilical cord and returns to the abdominal cavity. The proximal coils of jejunum leave the umbilical cord first

and pass from right to left behind the superior mesenteric artery. The postarterial segment, with the terminal ileum and cecum, then returns to the abdominal cavity and makes a counterclockwise rotation of 180 degrees from the left lower quadrant to the right upper quadrant.

Anomalies of Stage II: 1. *Nonrotation* is present when the gut is returned to the abdominal cavity from the temporary umbilical herniation but goes through none of the phases of rotation of the prearterial or postarterial segment. The duodenum descends along the right side of the abdomen, and the colon remains on the left. Usually there is no attachment of the mesentery of the small bowel to the posterior abdominal cavity when nonrotation occurs. 2. *Duodenal obstruction*, of an acute or a chronic type, occurs from one of two causes or from a combination of the two. When partial or incomplete rotation of the postarterial segment occurs, the cecum comes to lie in the midepigastrium and at that point puts out its peritoneal attachments, as though it were going to fix itself in the normal right lower quadrant. In so doing, the bands press upon the duodenum and produce obstruction. The second method by which this can occur is for the incompletely rotated midgut to volvulize upon itself and produce obstruction. This is possible because of the failure of attachment of the mesentery in the incompletely rotated intestine. 3. Fixation of the midgut anywhere along its rotational course may trap some coils of intestine and lead to an *internal hernia* in this way. 4. *Reverse rotation* is that condition in which the colon is found behind the superior mesenteric artery and the duodenum in front of it. The postarterial segment returns to the abdominal cavity first and rotates in a counterclockwise direction for 180 degrees, allowing it to go behind the artery; the duodenum follows and passes anterior to the artery.

Stage III (twelfth week to birth).—During this stage the cecum is thought to descend into the right lower quadrant from its position of right upper quadrant, with an orderly fusion of the mesentery to the posterior parietal peritoneum and a fixation of the duodenum, cecum, and ascending colon.

Anomalies of Stage III: 1. *A subhepatic cecum* can result very easily from failure of descent and elongation of the cecum in the third stage. This is frequently accompanied by failure of the small-bowel mesentery to attach, which will allow for the possibility of volvulus. 2. *A retrocecal appendix* results from the appendix being drawn underneath the cecum as it descends to the right lower quadrant. 3. Finally, *a mobile cecum* can occur when there is the normal descent of the cecum but failure of attachment to the posterior abdominal wall. This can and does result in volvulus of the cecum from time to time.

Clinical Picture

Presentation of the clinical picture of malrotation is based on experience with 44 symptomatic cases, as seen between Jan. 1, 1940, and Dec. 31, 1957.

Not all anatomical malrotations are symptomatic. This is borne out by the fact that symptomatic malrotations between 1951 and 1957 numbered 31. During the same period of time the x-ray department reported 82 cases of malrotation as demonstrated by gastrointestinal series.

Sex.—In the group of 44 patients there were 27 male and 17 female children. This corresponds with the generally stated incidence of a male preponderance in this pathologic condition.

Color.—As with other congenital abnormalities, the white race is most frequently

TABLE 1.—*Age Incidence at Surgery*

Age		
0-7 days	24 (55%)	80%
8-30 days	11 (25%)	
1-12 mo.	3	
1-5 yr.	4	
6-15 yr.	2	

TABLE 2.—*Presenting Complaints*

Vomiting		38 (86%)
Acute	24	
Chronic	14	
Pain		3
Melena		3

affected. In this series, there were 42 white children and only 2 colored children.

Age.—Table 1 summarizes the significant facts relative to the age incidence of symptomatic malrotation. This is predominantly a surgical condition of the first 30 days of life. Of the patients seen, 55% were problems of the newborn, occurring in the first seven days of life, while an additional 25% occurred in the next three weeks of life. The total incidence in the first 30 days of life was therefore 80%.

Weight.—Contrary to experience in some other congenital anomalies, malrotation does not seem to have a predilection for or cause prematurity. Only one of the symptomatic patients weighed under 5 lb. (2268 gm.).

Presenting Complaint.—Table 2 reveals that there were only three presenting complaints in this condition. Vomiting, either acute or chronic, was the chief complaint in seven out of every eight cases. Pain, unassociated with evidences of obstruction, was the paramount symptom in three patients, and the admitting cause was a bloody stool in three additional patients.

Associated Anomalies.—There was a total of 44 associated anomalies in this series of cases, and they are listed in Table 3. It is coincidental that the number of associated anomalies and the total number of patients are the same. Many of the patients had no associated anomalies, whereas others had several in addition to the malrotation.

The four anomalies that are of statistical significance include volvulus of the midgut which was present in 45% of the malrotations, duodenal stenosis and diaphragmatic hernia, which were each present in an additional 11% of cases, and, finally, an internal hernia, which presented in three patients.

Diagnosis.—The typical patient who is suffering from malrotation of the midgut is one in the first month of life who presents as an acute or chronic vomiter, with bile in the vomitus. The vomiting may be a tip-off to the presence of acute intestinal obstruction, or it may be reflective of a chronic, intermittent obstruction. Because of the age of the majority of children suffering from this condition, abdominal pain is difficult to assess; but in a few cases there will be the story of the child having passed some blood per rectum, usually indicating that there has been, or still is, a volvulus present. The volvulus may be suspected on physical examination by the palpation of a mass in the abdomen. In the face of vomiting of the degree and duration that usually accompanies this problem, the signs of a lowered sodium, potassium, and chloride, with an elevated CO_2, are found on electrolyte determinations.

In the minority of cases, an older child will present himself with the story of chronic abdominal pain, associated with nausea and vomiting at the time of pain. The child is quite often underdeveloped and lags behind in his growth patterns. Occasionally one sees a child with a celiac-like syndrome that can be attributed to a malrotation, although this is the rare type of picture leading to the diagnosis of malrotation.

The vast majority of cases of malrotation require the services of a roentgenologist to

TABLE 3.—*Associated Anomalies*

Volvulus	20
Duodenal stenosis	5
Diaphragmatic hernia	5
Internal hernia	3
Megacolon	2
Ileal stenosis	2
Jejunal atresia	1
Rectal stenosis	1
Absence of spleen	1
Atresia of colon	1
Omphalocele	1
Meckel's diverticulum	1
Duodenal atresia	1

establish the diagnosis. In complete intestinal obstruction, there will be a paucity or an absence of gas beyond the duodenojejunal junction. This is about all that one will find, since the stomach decompresses itself each time the child vomits and there are no distended loops of bowel present. In the infant, or older child with incomplete intestinal obstruction, one again will find a paucity of gas below the ligament of Treitz, as very little gas is able to get by the partial obstruction. In both these groups of cases, an upper gastrointestinal series is generally resorted to in order to secure the diagnosis. We have found that the administration of a water-soluble barium product (Dionosil, a propyl ester of 3,5-diido-4-pyridone-*N*-acetic acid) will reveal an obstruction in the duodenum, usually in the second or third portion. Proximal to the obstruction there will be a dilatation of the duodenum, with a "churning" action when viewed fluoroscopically. In most cases there will be a straight descent of the duodenum on the right side of the abdomen instead of the conventional curve to the left with left-sided duodenojejunal loops.

There are those who feel that the administration of a barium enema will always make the diagnosis in malrotation. It would seem fair to say that an upper gastrointestinal series is more important, for one is interested in whether there is obstruction present or not. Simply finding a colon that stops in the midepigastrium does not in itself indicate that there is an obstruction associated with it. This viewpoint is substantiated by the number of positive x-ray examinations that are clinically asymptomatic.

Differential Diagnosis.—1. Pyloric Stenosis: Symptoms in this condition generally come on a bit later in life than malrotation, although they can appear as early as the first 30 days of life. Vomitus in pyloric stenosis almost never contains bile, and with the aid of x-rays one can outline a distended stomach with an elongated, narrow pyloric channel that has "shouldering" at either end.

2. Duodenal Atresia: This is always a newborn problem in which there is continuous vomiting that may or may not have bile, depending upon the atretic site relative to the ampulla of Vater. With the aid of x-rays, one can determine that there is no gas distal to the point of atresia, a finding which is not generally true of malrotation.

3. Duodenal Stenosis: This is a very difficult condition to differentiate from malrotation and, as one can see from Table 3, it is associated with malrotation in a small number of cases (11%). X-rays, once again, will be of aid in suggesting a partial obstruction in the second or third portion of the duodenum, and oftentimes exploratory laparotomy is the only way of making the differential.

4. Duplication: This condition may present as a vomiting problem at any age, and one can usually feel a mass. There may be the presence of melena. Once again we must seek roentgenologic help to ascertain whether there is extrinsic pressure upon the intestinal wall in the area of the upper small intestine.

5. Jejunal or Ileal Atresia: The differential point here lies in the flat plate of the abdomen, which will show distended loops of small bowel with air-filled levels above and complete absence of gas below the point of obstruction. This is not the usual picture in a malrotation.

6. Annular Pancreas: Since this condition is so often associated with duodenal stenosis or duodenal atresia, it may present a very real difficulty in differential diagnosis. Complete absence of gas beyond the point of the second or third portion of the duodenum may suggest the presence of an obstruction other than malrotation, but, once again, exploratory laparotomy frequently is necessary to make the distinction.

7. Intracranial Lesion: Associated coma, restlessness, and vomiting with the absence of bile may be suggestive of the extreme forms of intracranial disease. Signs of in-

creased intracranial pressure and other localizing manifestations of a lesion may be helpful as well. Subdural taps or a spinal tap can be very useful in differentiating this condition from malrotation.

8. Paralytic Ileus: This is usually secondary to some infection elsewhere in the child, which will be manifest by fever, leukocytosis, and absence of peristalsis. The source for this infection should be sought for in omphalitis, respiratory disease, or urinary tract infection. X-rays will show dilated loops of intestine uniformly distributed throughout the abdomen with no signs of localized obstruction.

9. Meconium Ileus: This is oftentimes a familial disease in which other siblings or ancestors will give the history of newborn intestinal obstruction or mucoviscidosis. X-rays of the abdomen here will usually show the shadows of adult-like feces, which the normal newborn does not have. Small calcifications in the abdomen by x-ray are also suggestive of meconium ileus.

10. Megacolon: This is a low intestinal obstruction in most cases and therefore will show much distention throughout the gastrointestinal tract down to the rectosigmoid. A judiciously administered barium (or Dionosil) enema will frequently delineate the zone of aganglionosis, just as it does in the older child.

Dangers.—There are two dangers to a malrotation of the midgut, both centering around intestinal obstruction. A simple intestinal obstruction can occur at the duodenum from bands extending from the cecum to the right upper quadrant when the mesentery of the cecum fuses in the midepigastrium. Another cause of a simple obstruction may be failure of the prearterial segment to rotate in a normal fashion behind the superior mesenteric artery; it may become kinked under the peritoneal attachments in the second or third portion of the duodenum. Both these causes are important but do not involve the danger of encroachment on the blood supply of the bowel.

The most important risk of improper rotation of the midgut is volvulus. This may occur because of the lack of fusion of the mesentery of the small bowel when the rotational process of the midgut does not go on to completion. Under ordinary circumstances, the attachment of the small-bowel mesentery is from the left upper quadrant to the right lower quadrant, and in the absence of this attachment the entire small bowel is capable of volvulus. Simple volvulus contains only the danger of obstruction, but a more complete volvulus may end in gangrene of a large portion of the small intestine. Such a situation would reduce the child's chances for survival to almost zero.

Pathologic Anatomy

Table 4 indicates our various pathologic findings in this series. The outstanding anatomical finding was that in which the colon was found in the midepigastrium with complete nonattachment of the small bowel; this was present in 38 out of the 44 cases and represented one of the anomalies of Stage II development. Three cases had no attachment at all of either the colon or the small bowel, and these cases were representative of another Stage II abnormality. Another abnormality of Stage II occurred in two cases in which there seemed to be a normal distribution of the colon, but there were appearances of obstruction at the duodenojejunal junction from a failure of rotation of the prearterial segment. Finally, one case showed a high, mobile cecum, which would represent an abnormality of the embryonic development in Stage III.

Treatment

Preoperative Treatment.—Since all of these children are presented to the surgeon

TABLE 4.—*Pathologic Anatomy Found at Surgery*

No attachment of intestine	3 (7%)
Midepigastric cecum, unattached small bowel	38 (86%)
High, mobile cecum	1 (2%)
Normal colon, duodenojejunal obstruction	2 (5%)

because of intestinal obstruction, it is important to determine the electrolyte pattern prior to any surgery. In addition to a complete blood count and urinalysis, we routinely determine sodium, potassium, chloride, and CO_2, as well as make an estimate of the state of hydration. Replacement therapy is based upon the chemical determinations, and this is done as rapidly as convenient so as to shorten the time before operative relief of the obstruction. This reconstitution is usually carried out through a cut-down that has been placed in the saphenous vein, approximately 1 cm. below the saphenofemoral junction in the groin. The catheter is threaded up into the vena cava in order to utilize this means of doing a preoperative blood volume. A blood volume has been very helpful in view of the fact that the procedure itself is one in which considerable blood may be lost, and the radioactive-chromium tagging of cells gives us a ready means of knowing where we stand as far as blood replacement is concerned. The child is given ascorbic acid (vitamin C) and vitamin K parenterally if it is in the newborn period.

Operative Treatment.—Whenever the abdomen is opened in the case of malrotation, there are three points to be considered in operative technique. First of all, one must ascertain whether there is any volvulus present and reduce it or resect it. Second, if the colon is malpositioned, with the cecum in the epigastrium or the right upper quadrant, the peritoneal bands of attachment must be released. Third, complete examination of the duodenum, with release of any bands that are kinking it, must be carried out. Failure to follow these three orderly steps will result in an incomplete operation, and one which is doomed to postoperative complications and probably further surgery.

In 1936, Ladd[3] reported the procedure which now bears his name, and which is carried out by all those who see malrotation of the midgut; the complete Ladd procedure embraces the three above-mentioned steps. It was used alone or in combination with some other type of anastomosis or resection in all except 3 of the 44 cases reported here; it was difficult to ascertain from the operative notes in the 3 remaining cases whether it was used or not. Table 5 summarizes the methods of treatment used.

TABLE 5.—*Methods of Treatment*

Ladd procedure alone		31
Ladd procedure and bypass anastomosis		8
Duodenojunostomy	6	
Jejunojenostomy	1	
Ileoileostomy	1	
Ladd procedure and resection (volvulus)		2
Resection & anastomosis		3
Jejunal atresia	1	
Ileal stenosis	2	

Postoperative Treatment.—Well-planned mouth feedings generally have to be used to get the child started on the oral route of nutrition. It can usually be initiated within 72 hours of surgery, and we have found a pyloric-stenosis type of routine to be helpful. It has been our custom to follow the chemistry determinations during this "nothing-by-mouth" interval and maintain the electrolytes by intravenous methods. A blood volume determination is done the day after surgery, and any additional compensation for blood loss carried out on the basis of it.

Results

Mortality figures, as far as malrotation is concerned, have been surprisingly low in those series which have been reported. The largest series is from the Boston Children's Hospital,[4] in which their over-all mortality was 23%. An exactly similar mortality figure was reported by Snyder and Chaffin[5] in a series of 40 cases from the Los Angeles Children's Hospital. The results at the Children's Hospital at Pittsburgh are tabulated

TABLE 6.—*Mortality*

Alive	32 (73%)
Dead—hospital	9 (20%)
(From malrotation or complications)	
Dead—nonhospital	3 (7%)
(From late, unrelated causes)	

TABLE 7.—*Causes of Death*

Hospital	
1. Pneumonia, incomplete heart rotation, omphalocele and diaphragmatic hernia	
2. Peritonitis from perforation of ileum at operation	
3. Secondary gangrene from recurrent volvulus; died at secondary operation	
4. Adhesions, debilitation, partial obstruction; died at secondary operation	
5. Colonic atresia showed up postoperatively; secondary ileostomy with debilitation	
6. Volvulus and resection for gangrene at first operation	
7. Internal hernia with gangrene leading to resection and anastomosis at first operation	
8. Peritonitis from cecal perforation in reducing volvulus	
9. Thrush & debilitation in a case of resection for associated atresia	
Nonhospital	
1. Celiac disease, five years postoperative	
2. Strangulated internal hernia, one month postoperative, at home	
3. Recurrent diaphragmatic hernia at home	

in Table 6, with an over-all mortality figure of 27%. If one leaves out the three nonhospital deaths that were unrelated to the malrotation per se, there were nine deaths in 41 cases (22%).

Table 7 summarizes the causes of death in the hospital and nonhospital cases.

Comment

In any consideration of malrotation of the midgut, the problems encountered divide themselves into two general categories. There are those which are associated with the diagnosis and preoperative management of the situation and those which are peculiarly the concern of the surgeon doing the operation.

In almost all reported series, four out of every five cases of malrotation occur in the first 30 days of life. Some are acute problems which no one would be likely to miss because of their obstructive factors, and some are chronic, nagging vomiters who tax the acumen of even the best pediatricians. Fortunately, this is a condition that yields to the diagnostic ability of the roentgenologist in a high percentage of cases. It used to be thought that a barium enema was diagnostic for this condition if it showed the colon to be in an abnormal position, particularly with the cecum in the midepigastrium. It has become increasingly apparent that this is not so, and that the important thing is whether there is obstruction in the second or third portion of the duodenum. Malrotations show the disposition of the small bowel to be essentially on the right side of the abdomen with partial or complete obstruction, as opposed to the normal left position. One can have a malpositioned cecum and the child asymptomatic; it is also possible to have a child who has a normally disposed colon, but one who has obstructive difficulty from abnormalities of the prearterial rotation. It therefore would seem far better to make wider use of the upper gastrointestinal series after a supine and erect film of the abdomen without radiopaque material. Oftentimes a suggestion of the presence of malrotation can be obtained from the plain films alone if the colon seems to be in an abnormal position and there is a paucity of gas in the small-bowel loops, indicating a partial, high intestinal obstruction. Without the aid of the x-ray department, therefore, one would not arrive at a diagnosis in most of these cases.

Another fact that is well for pediatricians to bear in mind is that approximately one-half of the cases of malrotation also have an associated volvulus. Because of this, there is urgency to surgery in these cases. One is unable to tell from an external examination whether volvulus is present or not, and, if it is, whether it is of such a degree as to compromise the vascular supply of the bowel. It is therefore safer in all of these cases to have as short a period of preoperative preparation as possible.

To surgeons it must be emphasized that any given malrotation is seldom, if ever, identical with its predecessor. If one is looking at an abdomen which contains one of these abnormalities for the first time, it can present a very confusing picture. The commonest variety of abnormality occurs with the cecum fixed in the midepigastrium, with or without a volvulus. Simple reduction of the volvulus, by a clockwise or coun-

terclockwise rotation, is only a part of the operation. The final criterion of successful relief of the obstruction is to be able to follow the duodenum through its entire course down into the upper jejunum, being sure that there is no obstruction from volvulus, cecal bands, or intrinsic duodenal bands themselves. Having done this, one can rest assured that the operation will be successful in a high percentage of cases.

As in most congenital abnormalities, malrotation carries with it a high incidence of associated anomalies. The presence in this series of duodenal stenosis, megacolon, internal hernias, gastrointestinal atresia, omphalocele, Meckel's diverticulum, and the like is duplicated in the experience of all of those who see any number of malrotations. This only points up the fact that it is necessary, when examining the open abdomen, to be sure that there is not a coincidental anomaly present which is of importance equal to or greater than the malrotation itself.

Finally, it is very frequently stated that there is a marked association between diaphragmatic hernia and malrotation. This is of interest to the surgeon principally as it raises the question whether these hernias should be corrected through the abdomen or across the chest. Experience with the dual entities in this series is once again typical of what one reads in the literature; there were 5 cases of malrotation in the 31 cases of diaphragmatic hernia which came to surgery. This 16% incidence is high and argues for the abdominal route of approach in a newborn child. However, it is certainly an easier operation done transthoracically, and in the child with a diaphragmatic hernia who is beyond the neonatal period and who has shown no signs of obstruction, it would still seem to be the route of choice.

Summary

A series of 44 cases of malrotation of the midgut is analyzed.

The embryologic background, clinical picture, and treatment depict the condition as a pathologic process of the first month of life, diagnosable by x-ray, and needing early correction by surgery.

The mortality rate in uncomplicated malrotation should be 10%-15%. The mortality rate of 22% reported here compares favorably with that in other large series. Death was due in most cases to associated lethal congenital abnormalities.

Dr. David Clare, Dr. E. S. A. King, Dr. John J. McAleese, and Dr. William K. Sieber permitted us to include their cases in this paper.

Children's Hospital, 125 De Sota St.

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DISCUSSION

DR. JOHN L. KEELEY, Chicago: Dr. Kiesewetter and Dr. Smith are to be congratulated on this very fine presentation. They have a large and well-studied series, and the anomaly certainly is an interesting one.

Our own experience is much less extensive, but I believe it may justify a few remarks, which I should like to make in company with this series of slides.

(Slide) We thought at first that there had been a mistake in the x-rays that are shown here, but we found that the condition was a malrotation in a patient with situs inversus. The dilated stomach and duodenum are shown on the left, and a little contrast medium was used to outline the compressed duodenum on the right. This obstruction is incomplete, as Dr. Kiesewetter has already pointed out, and gives a little gas pattern in the lower part of the bowel; still, there was very little of the contrast medium that escaped in this particular patient.

(Slide) We have used barium enema for the establishment of the diagnosis in many of these cases. It will show the abnormal location of the ileocecal area, and it also shows that there need be no question about the patency of the large bowel at the time of the operation.

In the middle diagram we have tried to trace the course of the barium as outlined fluoroscopically. It does show this ileocecal area on the left upper quadrant instead of the right upper quadrant, as is usual, of course.

(Slide) Most of our patients have had duodenal obstruction as their outstanding feature; so we have shown here what amounts to a mirror image of some illustrations that you undoubtedly have seen before.

Simply dividing the bands, as has been mentioned, will solve the problem of duodenal obstruction, but we have made a practice of "reading" the entire small bowel to make sure we can pass gas through it, so that we do not overlook additional sources of obstruction. Certainly one would not fail to find a volvulus if that practice were followed; the other point is that we have already proved the patency of the colon. We need follow the bowel, then, only down to the ileocecal area.

(Slide) This shows a patient with this unusual combination of anomalies. One of the reasons we shall continue to have problems of this kind in increasing numbers is the practice (which certainly needs emphasis) of having a flat film taken of every newborn infant and every baby who is not doing well. A film of that kind taken on the first day or two of life sometimes will disclose a lesion that is incompatible with life or that constitutes a serious threat to life.

Synchronous (Two-Team) Abdominoperineal Resection of the Rectum

ROBERT L. SCHMITZ, M.D.; PETER A. NELSON, M.D.; GERARD B. MARTIN, M.D., and HAGOP M. BOGHOSSIAN, M.D., Chicago

In 1939, Lloyd-Davies, of St. Mark's Hospital, London, England, reported that combined abdominoperineal resection of the rectum could be done by two surgical teams working synchronously.[12] He mentioned in his article that "both Kirschner and Devine have developed methods on similar lines," but he gave no details and no references.

Since this first report, the operation has grown in popularity in the British Isles [9,13] and has found advocates in Europe,[1,3,7] South America,[5,6] and the United States of America.[4,11,14]

Most surgeons apply the two-team technique only for resection of the rectum, but Howkins, of London, uses it for radical hysterectomy,[10] and Canónico, of Buenos Aires, for pelvic exenteration.[5,6]

Most of these reports deal with the details of the technique and its advantages and disadvantages: they do not include comparative studies.

In 1949, Warren Cole, of The University of Illinois, reported to the Chicago Surgical Society the highlights of a clinical trip to England. He had observed the two-team technique at St. Mark's Hospital and was very impressed with the possibilities. His enthusiasm encouraged us to try it; we have been very pleased with it and feel that a critical comparison with the one-team technique is in order.

Material

We have used synchronous abdominoperineal resections in 37 instances (Table 1). The majority were done for carcinoma of the rectum (26), but the procedure was also employed for carcinoma of the genitalia and of the bladder and in two cases of chronic ulcerative colitis for which the rectum was excised as a separate-stage operation.

Positioning the Patient

No special tables, rests, or leg stirrups are used. (This is not to say that they might not be helpful.[9,12,14]) The patient is put to sleep in the supine position. Inhalation anesthesia has been administered in all instances, but spinal anesthesia would not alter the technique.

TABLE 1.—*Synchronous Abdominoperineal Operations*

Site of Primary Disease *	Organs Resected	No. of Cases: Individ.	No. of Cases: Total
Rectum	Rectum only	22	28
	Rectum+genitalia	4	
	Rectum+retroperitoneal sarcoma	1	
	Posterior exenteration	1	
Sigmoid †	Total exenteration	1	1
Bladder	Anterior exenteration	2	2
Cervix	Anterior exenteration	2	6
	Posterior exenteration	3	
	Total exenteration	1	
Total			37

* All cancer except two cases under rectum of chronic ulcerative colitis.

† Recurrence in cul-de-sac and vagina after resection of Ca of sigmoid.

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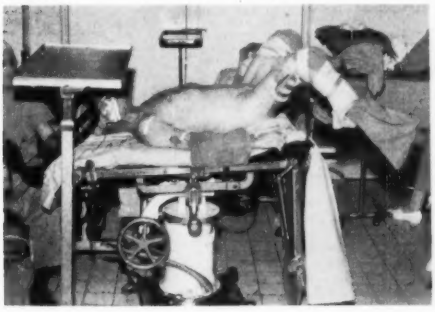

Figure 1

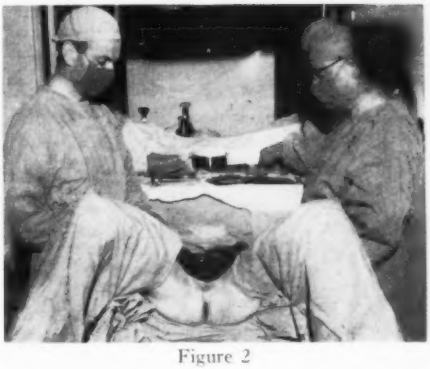

Figure 2

Once asleep, the patient is placed in the lithotomy position, with the thighs flexed 45-60 degrees at the hips and the legs flexed 80-90 degrees at the knees (Fig. 1), with the extremities widely apart and the pelvis elevated off the table by a sandbag or folded blanket under the sacrum (Fig. 2). Then the table is tilted 10-20 degrees into the Trendelenburg position, and a large instrument table is placed over the head end, respecting the anesthesiologist's room as much as possible (Fig. 1).

A bag catheter is inserted into the bladder and fastened high on one thigh, with a rubber glove over the end to catch the discharge of urine. In the male, the external genitals are elevated from the perineal field with a moist towel looped beneath them and across the groins (Fig. 2). The patient is covered with sterile half-sheets in such a manner that the abdominal and perineal fields are continuous.

There is sufficient room for an abdominal team of two or three surgeons and an instrument nurse, and a perineal team of two surgeons and an instrument nurse.

Operative Technique

The abdomen is opened through a left paramedian incision. As soon as exploration has established the operability of the lesion, the perineal team places two purse-strings of heavy silk about the anus to prevent fecal discharge during manipulation. At the same time, the abdominal team ties off the appropriate blood vessels above, viz., the superior hemorrhoidal artery and vein, or the inferior mesenteric artery and vein, and the hypogastric arteries.

After that, both teams work simultaneously, and, as the dissections approach each other, it is easier to identify cleavage planes and landmarks, such as the rectovaginal and vesicovaginal septa, Denonvilliers' fascia, the ureterovesical junctures, the uterine vessels, and the lateral rectal ligaments and middle hemorrhoidal vessels. Especially in bulky tumors is the dissection simplified.

Usually the dissection along the posterior cleavage planes is completed first and then the dissection anteriorly, and finally the lateral attachments are divided, with the two teams cooperating on such structures as the lateral ligaments of the rectum with the middle hemorrhoidal vessels, the uterine vessels, and/or the ureterovesical junctures. During the operation hemostasis is easier, since a bleeder difficult for one team to reach is usually readily available to the other. Often it is easier for one team to clamp a bleeder and for the other team to tie it.

After the tissues to be removed are completely mobilized, they are passed upward into the abdomen and then out through the abdominal incision. Formerly we kept the bowel intact until the abdominal wound had been closed around it and then amputated the specimen to establish the colostomy. Now, however, we are constructing flush skin-to-mucosa colostomies in the left lower

quadrant, and the sigmoid must be transected before the abdominal wound is closed so that the proximal end can be passed through a separate small opening in the abdominal wall.

After the pelvis has been emptied, the peritoneal floor is readily reconstructed. The abdominal and perineal wounds are closed simultaneously. Except for unusual bleeding, no packs are used; instead, a bundle of three or four Penrose cigarette drains is left in the hollow of the sacrum, protruding through the posterior wound, which is closed snugly about it.

In uncomplicated carcinoma of the rectum in males, that organ alone is resected; in females, we almost routinely resect the entire rectovaginal septum, and, in anterior-wall tumors, the uterus, tubes, and ovaries in continuity as well.

Evaluation of Two-Team Technique

While our clinical impressions of the synchronous two-team operation were very favorable, we felt that we should try to measure its value more objectively.

From 1946 through 1956 we did 22 abdominoperineal resections of the rectum for carcinoma by the one-team technique. From 1950 through mid-1957 we did 24 such resections by the synchronous two-team technique (Table 1: The two done for chronic ulcerative colitis and the two with additional major procedures are excluded, for obvious reasons). These two series are not ideally comparable. Most of the one-team procedures were done prior to 1950; all of the two-team procedures were done after 1950 (Fig. 3). In the latter period there were certain improvements in the use of antibiotics in the preoperative preparation and in the postoperative treatment of complications. The surgeons' skill was improving with experience. There was a shift at our hospital in 1951 from all nurse anesthetists to all medical anesthesiologists and among the effects of this shift was the use of more blood transfusions during the operations, since a better effort was made to measure blood loss and to replace it rather exactly.

Nevertheless, the types of patient comprising the two series match rather well (Table 2), and it was felt that a comparison of them might yield significant information.

There was an average saving of 45 minutes in operating time with the two-team operation (Table 3), a saving which was not unexpected, of course. It is interesting that the average time for the two-team procedure (1 hour 50 minutes) was less than the shortest time for any of the one-team operations (1 hour 55 minutes). We appreciate that speed is not necessarily of major importance, but it is always worth

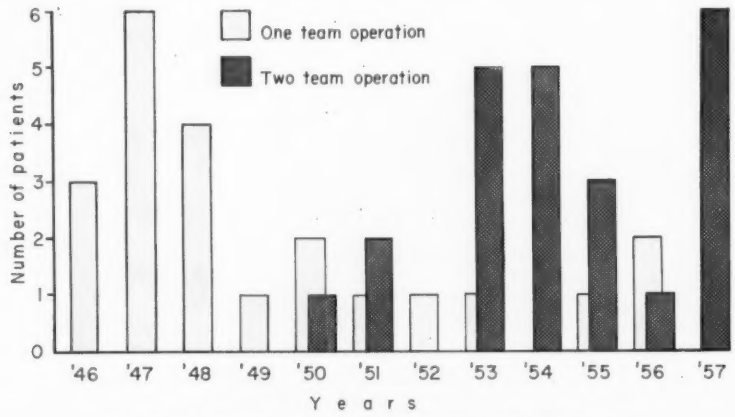

Fig. 3.—Chronology of operations for cancer of the rectum.

TABLE 2.—*Comparison of Patients Operated on for Carcinoma of Rectum*

	One Team	Two Team
No. of cases	22	24
Youngest	32	46
Oldest	75	76
Average age	59	62
Males	8	8
Females	14	16
Rectum only resected	20	20
Rectum+genitalia resected	2	4

TABLE 3.—*Operative Time*

Hours	1-1½	1½-2	2-2½	2½-3	3-3½	3½-4	Average Time
One team *		5	7	4	4	2	2 hr. 35 min.
Two team †	9	7	8				1 hr. 50 min.

* Shortest = 1 hr. 5.5 min.; longest 3 hr. 50 min.
† Shortest = 1 hr. 0.5 min.; longest 2 hr. 30 min.

while if good surgical principles are not compromised to gain it.

The amount of whole blood transfused to the two groups during surgery was essentially the same (Table 4), although two of the one-team patients were given plasma in addition. That the two-team group did not receive *less* blood may be accounted for by the more careful replacement practiced by the medical anesthesiologists, as previously stated. On the other hand, that they did not receive *more* blood speaks against the two-team procedure being more shocking than the one-team approach, as has been suggested by Aylett.[2] The operative courses in the two-team cases were smoother, as judged by the records of the vital signs and the anesthesiologist's notes (Table 4).

Postoperatively, the two-team patients stayed three days longer on the average, but three of these patients had additional surgical procedures during the stay (two transurethral prostatectomies and one resection of a solitary pulmonary metastasis), while only one of the one-team patients had an additional procedure (a transurethral prostatectomy) (Table 5).

The two series had about the same number of postoperative complications, but only one of the two-team complications was fatal, while four of the one-team complications were (Table 5). The various complications are listed in Table 6, and the fatal ones are indicated. As usual, the two greatest problems were urinary retention, with its related features, and pulmonary embolism. This experience parallels that at the University of Iowa in a much larger series, where the mortality rate for abdominoperineal resection of the rectum dropped from 9.6% to 3% with the adoption of the two-team operation.[4] Obviously, other factors were involved as well.

There are some disadvantages to two-team operations, but they are minor ones. Two skilled surgeons and their assistants must be at hand. This is no problem in teaching centers, larger medical groups, or surgical partnerships, but the operation may present some difficulty for the surgeon alone in private practice. There is some crowding of both the abdominal and the perineal fields from the position of the patient's legs, but adjustment is not hard. There is a greater danger of trauma and blood loss when two surgical teams are working simultaneously,[2] so that it is important that they observe carefully good surgical principles, especially in regard to the gentleness with which tissues are handled and to hemostasis.

It is our feeling from the evidence presented that the two-team operation has ad-

TABLE 4.—*Operative Course*

	Blood Given, Pints							Vital Signs	
	0	1	2	3	4	6	Ave.	Stable	Unstable
One team	1	7 *	9 †	2	2	1	2.05	12	10 (45%)
Two team	0	6	11	4	3	0	2.17	17	7 (29%)

* 1 had 500 cc. of plasma also.
† 1 had 1000 cc. of plasma also.

TABLE 5.—*Postoperative Course*

	Postoperative Stay, Days *									
	8–14	15–21	22–28	29–35	36–42	43–49	50–56	Ave.	Complications	Hospital Deaths
One team †	5	3	6	2	..	..	2	28+	8†	4
Two team ‡	3	6	3	4	4	4	..	27±	9‡	1

* Excluding patients who died in hospital.
† One patient had secondary operation: TUR (transurethral prostatectomy).
‡ Three patients had secondary operations: TUR two; resection solitary pulmonary metastasis, one.

vantages over the one-team procedure and that it should be more widely used. It is of particular value in the treatment of bulky pelvic tumors, and we are employing this approach more and more in pelvic exenterations for genital cancer. It should also lend itself in modified form to the surgery of chronic ulcerative colitis, polyposis, imperforate anus, and Hirschsprung's disease (megacolon).

TABLE 6.—*Complications*

Type	One Team	Two Team
Urinary retention	3 *	4 †
Pulmonary embolus	3 ‡‡	1
Dehiscence	1	1
Pyelonephritis	1 ‡	
Lower nephron nephrosis		1 ‡
Cerebrovascular accident		1
Adrenal insufficiency		1
Total	8	9

* One required TUR (transurethral resection) for benign prostatic hypertrophy.
† Two required TUR for benign prostatic hypertrophy.
‡ Fatal complication.

Summary

Synchronous two-team abdominoperineal resections of various pelvic organs have been done in 37 instances.

The positioning of the patient, the operative technique, and the extent of the surgical procedures for removal of the rectum are discussed.

The two-team approach seems technically easier to the surgeons, especially in bulky tumors, allows more adequate hemostasis, and permits a better closure of the peritoneum over the empty pelvis.

Twenty-four two-team operations for rectal cancer are compared with twenty-two one-team operations for similar disease.

The two-team technique took 45 minutes less on the average, did not increase the amount of blood transfused, gave a smoother operative and postoperative course, did not increase the number of complications, and led to fewer deaths.

The disadvantages of the two-team operation are minor: the need for extra skilled personnel, the crowding of the operative fields, and the danger of increased trauma and blood loss.

We recommend that more surgeons try the synchronous two-team technique, especially in bulky or extensive cancers of the pelvic viscera, but also whenever a combined abdominal and perineal operation is necessary.

55 E. Washington St. (2).

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DISCUSSION

DR. HARRY S. MORTON, Montreal: The synchronized abdominoperineal resection which has been described by Dr. Schmitz was introduced by Dr. Campbell Gardner and me from England into Canada at the end of the war, in 1945, where we have been using it ever since. I would like to remark on the position. We do not flex the thigh on the abdomen, thus giving the abdominal surgeon more room, and perhaps cramping a little the fellow called "Tail-end Charlie." However, we still have a lot of room down below.

Second, the specimen, when finally freed, is removed through the lower end; so there is less contamination of the peritoneal cavity. I liken it to a train coming out through a tunnel.

Altogether, the ease of control, the ability to remove more tissue, and the lack of disturbance of the patient enable the surgeon to do a more extensive procedure, with, I think, better results. The operative mortality is lowered, and usually the morbidity is markedly reduced.

I thought, therefore, you might be interested in our five-year follow-up results. Of 250 cases that are available since 1945, only 124 before 1952 are eligible for the five-year follow-up results. Of these procedures, 57 were done by the synchronized combined method and 67 by the ordinary single abdominoperineal. A comparison of the five-year survivals, with no corrections of any kind, gave almost twice as many patients living with the combined method as with the single operation—56%, as compared with 30%.

Recently, cystectomy and removal of the pelvic viscera, along with ileobladder, have been done in 20 cases by this method, with no postoperative deaths.

I would like to congratulate Dr. Schmitz and his associates on bringing this procedure to the attention of this association.

DR. HAROLD LAUFMAN, Chicago: I, too, would like to congratulate Dr. Schmitz and his associates on reemphasizing a very useful procedure.

I was first exposed to this procedure in 1939 at St. Mark's Hospital in London. After doing the operation in a few cases with Dr. Ralph Bettman, we reported them in 1943 (Laufman, H., and Bettman, R.: One-Stage Radical Resection of the Rectum by Modified Lloyd-Davies Technic, *Am. J. Surg.* 60:243-247, 1943). I think today, however, with the paucity of help and the difficulties in finding an associate who knows perineal surgery, the greatest usefulness of the procedure, actually, lies in a one-surgeon operation.

Using this positioning, one surgeon can work from both above and below after he has dissected part of the pelvic portion of the operation, and in this way he can get a better evaluation of the extent of the tumor and can adapt the procedure to it.

So I think, therefore, the greatest advantage today for most of us is the versatility of the positioning in this procedure, although if one has two good teams it is still good as a two-team operation.

DR. DONALD M. GLOVER, Cleveland: I was first exposed to this method when stationed in Melbourne, Australia, in 1942, when Sir Hugh Devine was employing the two-team method of resection. It interested me sufficiently so that when I came back, I began using the method, and I have been more or less ever since.

As Dr. Morton has indicated, I also took some exception to seeing the anal end of the bowel brought up through the peritoneal cavity, and compromised by dividing the colon above and bringing the specimen out from the lower incision.

It is true that the procedure cuts down the operating time between 30 and 45 minutes in the average abdominoperineal resection. In order to give the resident greater experience, in the compromise method, I usually get the upper part of the section done abdominally first, and then drop down and do the perineal part while my resident-assistant completes the abdominal part. This is a compromise, but it makes it possible to do about the same sort of job and not upset the normal resident training mechanism.

Nature and Treatment of Septic Shock

WILLIAM A. ALTEMEIER, M.D., and WILLIAM R. COLE, M.D., Cincinnati

The occurrence of circulatory failure, falling blood pressure, and a shock-like state during a severe infection is a serious complication. Death is usually imminent within hours, and treatment is generally unsuccessful.

Shock, associated with sepsis, has been recognized for many years, having been described by Laennec in 1831 [1] and Boise in 1897.[2] More recently, Ebert [3] has emphasized the frequent occurrence of this complication on medical wards in relation to infections, and Davies [4] has described seven cases subsequent to ruptured abdominal viscera.

Relatively little is known concerning the pathologic physiology of shock associated with infection, and it is obvious that more detailed knowledge would be helpful in the search for any improvements in therapy.

A review of the published work [5-18] indicates that at least four factors may be concerned with its development.

1. A loss of fluid from the circulation, resulting from dehydration, persistent vomiting, continued diarrhea, or massive exudation into body cavities, may produce hemoconcentration and diminished blood volume.

2. A disparity may develop between the circulating blood volume and the capacity of the peripheral vascular bed caused by vasodilatation in the presence of a normal or nearly normal blood volume.

3. Failure of the peripheral circulation may be caused by the direct action of bacteria or their toxins on the capillary walls, by the effect of histamine-like substances on the vascular tree, or by the direct action of bacterial toxins on the heart.

4. The adrenal glands may be involved either indirectly by toxemia or directly by the infection.

Recently,[18] 93 fatal clinical cases of infection associated with shock were studied on the surgical services of the Cincinnati General Hospital and the University of Cincinnati between Jan. 1, 1951, and Nov. 16, 1955. Generalized peritonitis was the infection in 54%, intra-abdominal abscess in an additional 12%, and a miscellaneous variety of lesions, including cellulitis of the skin and subcutaneous tissues, enterocolitis, empyema, and mediastinitis, accounted for the remaining 34%.

The correct clinical diagnosis of septic shock had been made infrequently in this series. The principal reasons responsible for this appeared to be the surgeon's ignorance of the possibility of this complication and his overconfidence in the effectiveness of antibiotic agents.

Signs and Symptoms

The characteristic signs and symptoms noted in our review of these cases included the following:

1. The sudden, insidious, and unanticipated development of hypotension, tachycardia, cyanosis, urinary suppression, and other symptoms of severe circulatory collapse in a patient with fever

2. The occurrence of a shock-like state in the absence of the usual causes, such as hemorrhage or trauma

3. The presence of a serious infection whose presence may be obvious or obscured by the masking of localized symptoms by antibiotic therapy

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From the Department of Surgery, University of Cincinnati College of Medicine and the Cincinnati General Hospital.

Work done under contract with the Office of the Surgeon General, U. S. Army, and under the auspices of the National Research Council.

4. The sudden development of the signs of shock in a patient with a known intra-abdominal abscess

5. The failure of the state of shock to respond to the usual methods of treatment used for hemorrhagic or traumatic shock

6. The presence of a high white blood cell count, usually 20,000 or more, with a marked predominance of polymorphonuclear cells and evidence of toxic granulation. A very low white blood cell count may also be suggestive of an overwhelming infection

7. The presence of petechiae, unexplained delirium, or ileus

A review of the pertinent autopsy findings, other than those of the primary infection, revealed a high incidence of pulmonary edema, involvement of the adrenal glands in only 6%, and a surprisingly low incidence of lower nephron nephrosis in only 5%.

Method of Treatment

On the basis of these observations, the following plan of treatment was evolved and used during the past two years as soon as a diagnosis of septic shock was made.

1. Immediate intravenous infusion of fluids, particularly plasma or blood, was carried out in an attempt to correct any deficiency of the circulating blood volume without overloading the circulation.

2. Massive doses of antibiotics were administered by the intravenous route. The agents chosen for each case necessarily were often selected empirically until reports of bacterial cultures and sensitivity to the antibiotics were obtained. The existence of shock made the intravenous route advisable because of the impairment of absorption, the urgent need for a rapid therapeutic effect, and the overwhelming nature of the infection.

3. Arterenol was administered in 5% solution of dextrose in water by intravenous drip, regulated to restore the blood pressure to a level of 80 mm. Hg or above. This was done in an effort to maintain the various essential physiologic functions, particularly renal filtration, until the infection was brought under control. Since our previous study had called attention to the high incidence of pulmonary edema which occurred during the intravenous infusion of fluids given in a vain attempt to elevate the blood pressure, arterenol was used in conjunction with moderate fluid replacement to reestablish the blood pressure and to avoid this complication. It was discontinued only after the blood pressure could be maintained without it.

4. An indwelling catheter was used to measure the hourly urinary output, which was maintained between 25 and 75 cc. per hour, by the regulated administration of arterenol and fluid.

5. Oxygen was administered continuously by nasal catheter or tent.

6. The foot of the bed was elevated 12 to 18 in.

7. Cortisone or hydrocortisone was withheld unless it was impossible to restore or maintain the blood pressure by the administration of fluids and arterenol. Under this circumstance, the steroid hormones were used in an effort to extend the patient's life until the severe infection could be controlled by the intensive antibiotic therapy and any indicated surgical treatment.

8. Timed surgical intervention was carried out when indicated and feasible.

The purposes of this report are to reemphasize the frequency with which septic shock occurs in severe surgical infections and to describe our experiences with the above general plan of treatment.

Material

Between November, 1955, and November, 1957, an additional 41 patients with circulatory collapse which occurred in association with known and severe infections have been studied on the surgical services of the University of Cincinnati. Twenty-three patients were female and 18 were male. All of the 41 patients showed manifestations of severe infection, as well as those of profound shock with hypotension. None had any other known cause of shock, such as trauma, hemorrhage, or neurogenic stimuli. For purposes of discussion, the types of infection are listed separately for the fatal and

TABLE 1.—*Primary Diagnoses in Cases of Septic Shock*

Fatal Cases		Surviving Cases	
Generalized peritonitis:			
Perforation of colon secondary to carcinoma	6	Perforation of colon secondary to carcinoma	2
Perforation of intestine secondary to obstruction	5	Diverticulitis of colon with perforation	2
Perforated peptic ulcer	2	Perforated peptic ulcer	2
Ruptured tubo-ovarian abscess	2	Ruptured tubo-ovarian abscess	2
Ruptured appendiceal abscess	1	Ruptured appendiceal abscess	1
Hemorrhagic ileocolitis with perforation	1	Empyema of gallbladder with pericholecystic abscess	1
	17 (68%)		10 (63%)
Miscellaneous infections			
Hemorrhagic enterocolitis	3	Hemorrhagic enterocolitis	2
Retroperitoneal abscess	1	Pyothorax with septicemia	1
Acute hemorrhagic cystitis	1	Endometritis with septicemia	1
Gas gangrene of shoulder and thorax	1	Urinary extravasation with septicemia	1
Extensive cellulitis of leg	2	Extensive cellulitis of leg	1
	8 (32%)		6 (37%)

for the surviving cases in Table 1. They are similar for the two groups, peritonitis secondary to a variety of lesions being the responsible infection in over 60% in both groups. The remainder were miscellaneous infections, including gas gangrene, cellulitis of the skin and subcutaneous tissues, hemorrhagic enterocolitis, endometritis, and pyothorax.

The incidences of the various signs and symptoms which were observed are tabulated in Table 2. Of interest are the high incidences of fever, tachycardia, mental confusion, and cold clammy skin. The average body temperature in 38 of the 41 cases was 102.4 F. Three of the fatal cases seen terminally in a moribund state did not have a temperature recorded. The average systolic blood pressure at the time of diagnosis of septic shock was 50 mm. Hg. Cold clammy skin was noted more frequently than a hot dry skin, even though the body temperature was markedly elevated. Four of the patients were in coma, and one had convulsions during the period of hypotension.

The laboratory data recorded in the 41 patients at the time of hypotension have been averaged and compared in Table 3. An elevated white blood cell count was consistently found, only an occasional severe depression being noted.

TABLE 2.—*Signs and Symptoms in Cases of Septic Shock*

	Fatal Cases (Total 25)	Surviving Cases (Total 16)
Hypotension	25	16
Tachycardia	23	16
Elevated temperature	22	16
Cold clammy skin	21	10
Hot dry skin	1	1
Mental confusion	14	10
Cyanosis	7	4
Restlessness and apprehension	5	4
Lethargy	3	1
Coma	4	0
Chills	0	1
Jaundice	0	1
Convulsions	0	1

TABLE 3.—*Average Laboratory Data in Cases of Septic Shock*

	Fatal Cases	Surviving Cases
Temperature (F)	102	103.6
Pulse, count per min.	146	130
Hgb, gm. per 100 ml.	12	12.8
WBC, count per cu. mm.	26,950	22,000
BUN, mg. per 100 ml.	62.8	25.6
CO_2, mEq. per liter	19	21.2
Cl, mEq. per liter	93	99
pH	7.33	7.26
Na, mEq. per liter	128	131
K, mEq. per liter	5.4	4.2

TABLE 4.—*Autopsy Findings in Twenty-Five Fatal Cases Associated with the Primary Infection*

Pulmonary complications	
Pulmonary edema	8
Pneumonitis	5
Atelectasis	4
Miliary abscess	2
Pulmonary infarction	1
Fibrinous pleuritis	1
Liver	
Acute necrosis of liver	4
Acute toxic hepatitis	1
Spleen	
Acute splenitis	2
Kidney	
Pyelonephritis	2
Lower nephron nephrosis	1
Toxic nephrosis	1
Cardiovascular	
Myocarditis	4
Pericarditis	2
Septic thrombosis of aorta	1

Results of Treatment

Of the 41 recent patients treated in this manner, 16 survived and 25 died, giving a survival rate of 39%. The delay in recognizing the nature of the circulatory collapse and in instituting treatment was an important factor in this mortality. Three of the fatal cases were seen terminally, and death occurred within a matter of a few hours. In the 25 fatal cases the associated pathologic findings found at autopsy are listed in Table 4. These are similar to the pathology previously reported in our earlier study, and the incidence and importance of pulmonary edema, pneumonitis, acute hepatitis, and acute necrosis of the liver in the mortality are noteworthy.

The average level to which the systolic blood pressure fell in the surviving patients at the height of the infection was 50 mm. Hg, and in half of the patients the pressure fell to 50 mm. or below. The temperature at the time of circulatory collapse in this group varied from 101 to 107 F, the average being 103.6 F. The pulse was likewise rapid and often thready in this period, the average being 130 per minute, and the extremes being 90 and 160 per minute.

Variations in the white blood cell count at the time of hypotension were particularly interesting. As the blood pressure dropped precipitously, the temperature, pulse rates, and white blood cell counts rose sharply and characteristically. The average white blood cell count during the period of shock was 22,000, the highest being 47,800 and the lowest 3750. In only three cases was the count 8000 or below.

Studies to determine the presence of hemoconcentration as a basis for the hypotension also revealed interesting data. Four patients showed hemoconcentration, as manifest by a rise in the hemoglobin and hematocrit levels at the time of hypotension. Three of these had generalized peritonitis, and one had acute hemorrhagic enterocolitis. On the other hand, six showed evidence of a sudden fall in the hemoglobin to levels of 9 to 10.5 gm., suggesting hemolysis or hemodilution. These included two patients with septicemia, two with peritonitis, one with gas gangrene, and one with pseudomembranous enterocolitis. In the remaining six surviving patients, there was no significant change in the hemoglobin or hematocrit.

The moderate elevation in blood urea nitrogen and the tendency toward metabolic acidosis noted in these cases agree with our earlier observations [18] and those of Martin and Nichols.[19]

All of the 16 patients who survived were given antibiotic therapy intravenously for the treatment of the infection after onset of the shock. For periods varying from 6 to 10 or more days, all received aqueous penicillin G in large doses up to 1,000,000 units every three hours, and eight were given chloramphenicol. Tetracycline was administered to seven and erythromycin to two.

Fifteen of the sixteen patients received arterenol by intravenous drip at varying concentrations and rates to maintain a blood pressure of 80 mm. Hg or more. The dose of arterenol varied from 4 to 40 cc. per 1000 cc. of 5% solution of dextrose in water. The average duration of arterenol therapy was 57 hours, with a range of 3½ to 144 hours. The one treated without arterenol responded satisfactorily to the transfusion of blood and plasma.

Of the 16 patients, 11 received blood or plasma or both, the amounts varying from 500 to 4500 cc., the average amount transfused being 1000 cc.

In 3 of the 16 patients, it was necessary to give hydrocortisone in doses up to 100 mg. for additional support when the arterenol was found to be inadequate. The hydrocortisone was administered for 24, 60, and 72 hours, respectively.

In addition, 13 were given oxygen therapy over periods of 24 to 168 hours in an effort to minimize the effects of the associated cyanosis.

Under the above therapy the average duration of the period of arterial hypotension in the 16 patients who survived was 76 hours, the shortest being 12 and the longest 168 hours. With the continuing administration of arterenol and occasionally hydrocortisone, it was possible to keep the blood pressure at levels of 80-90 mm. Hg and urinary filtration at a rate of 25 cc. or more per hour. When the infection was brought under control, it was possible to maintain a normal blood pressure without the use of vasopressors.

The course and treatment in four of the surviving cases are reported here briefly to illustrate the principles and results of treatment used.

Case 1.—A., a 14-year-old girl, was operated upon for pyloric obstruction produced by a duodenal ulcer on May 14, 1955. Postoperatively, she received Dicrysticin,* streptomycin, and tetracycline. On her fourth postoperative day, there developed a temperature of 107 F, elevation of the pulse rate to 140 a minute, numerous watery stools, and circulatory collapse. At the same time, her white cell count rose from 7000 to 35,000 per cubic millimeter (Fig. 1). A diagnosis of hemorrhagic pseudomembranous enterocolitis caused by the hemolytic Staphylococcus aureus

* Crystalline procaine penicillin G fortified, 400,000 units, with hydrostreptomycin sulfate, 0.5 gm.

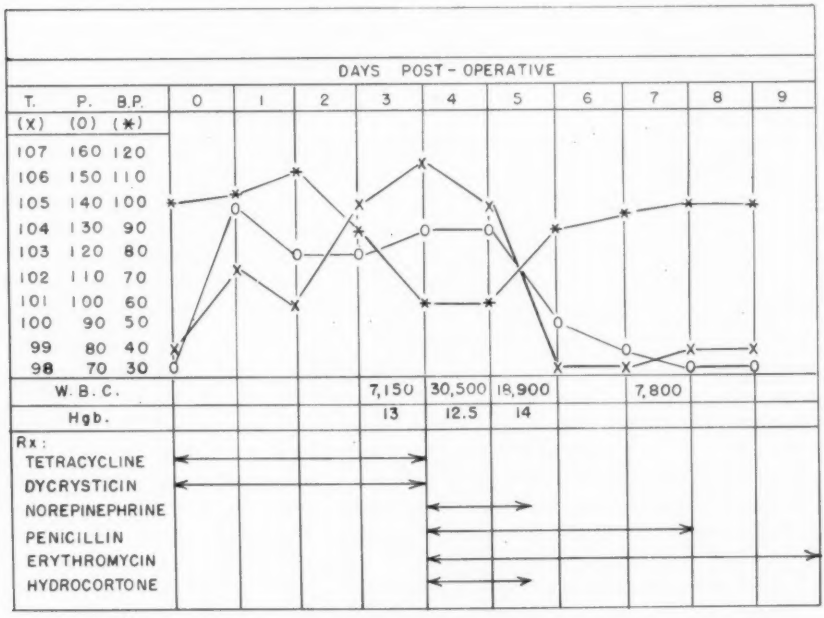

Fig. 1 (Case 1).—Course in a 14-year-old girl (A.), who developed shock during the course of a fulminating staphylococcal pseudomembranous enterocolitis. Note the elevated curves of temperature and pulse rate and the inverted curve of the blood pressure. Prompt treatment with discontinuation of tetracycline and the intravenous infusion of arterenol, erythromycin, blood, and hydrocortisone quickly reversed the process and permitted the complete and spontaneous recovery of the patient.

was made, and this organism was found in the stool on the smear and culture in great numbers. Tetracycline and streptomycin were discontinued promptly, and the patient was treated with erythromycin and aqueous penicillin G intravenously. She also was given arterenol and hydrocortisone by intravenous infusion to reestablish and maintain her blood pressure. The hydrocortisone was used when arterenol appeared to be inadequate. It was felt in this instance that its use was lifesaving in that it helped to tide over this critically ill patient until the full effect of the antibiotics could be obtained. The patient's temperature, pulse rate, and white blood cell count fell to normal in 48 hours; the blood pressure rose to a normal level in the same period, and the patient made a complete recovery.

CASE 2.—B., a 58-year-old woman, was admitted to the Cincinnati General Hospital in October, 1954, with a diagnosis of acute cholecystitis and empyema of the gallbladder. She was treated with intravenous fluids and prepared for operation because of the intensity of the infection and its failure to respond to conservative measures. Shortly before the induction of anesthesia, the patient's blood pressure fell rapidly and unexpectedly to 30/0 and her temperature rose to 104 F (Fig. 2). She was immediately treated with 600,000 units of aqueous penicillin G and 500 mg. of chloramphenicol, infused intravenously every six hours. Arterenol was given continuously in doses as high as 20 cc. per 1000 cc. of 5% dextrose in water for six days. The total 24-hour urinary output dropped to 400 cc. on the first day but thereafter was maintained at normal levels. The white blood cell count was 23,800 per cubic millimeter at the onset of the shock, and the patient had evidence of diabetes, as indicated by analysis of the urine and blood.

She received oxygen by nasal catheter but was given no blood or plasma for fear of overloading her cardiovascular system, which previously was known to be hypertensive. After restoration of her blood pressure, the patient was anesthetized, and a cholecystostomy with drainage of the abscess was performed. Postoperatively, it was possible to maintain her blood pressure and urinary filtration with arterenol and to control her infection by massive doses of sodium penicillin G and chloramphenicol given intravenously.

Culture of the pus obtained from the gallbladder revealed the presence of a hemolytic S. aureus and a bacillus of the coli-aerogenes group. Both organisms were sensitive to chloramphenicol.

CASE 3.—C., a 43-year-old Negro man, was admitted to the Cincinnati General Hospital in

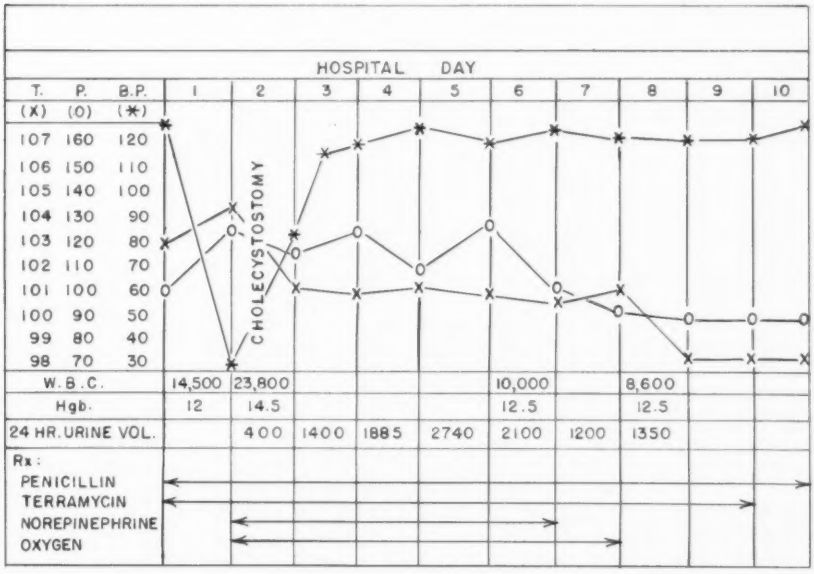

Fig. 2 (Case 2).—B., acute cholecystitis. This chart illustrates the rise of temperature, pulse rate, and white blood cell count at the time of a precipitous fall in blood pressure in a patient with empyema of the gallbladder and abscess caused by the hemolytic S. aureus. Cholecystostomy, with drainage of the abscess, was performed after beginning treatment for septic shock. Note temporary increase of hemoglobin during hypotension. The patient made a complete recovery.

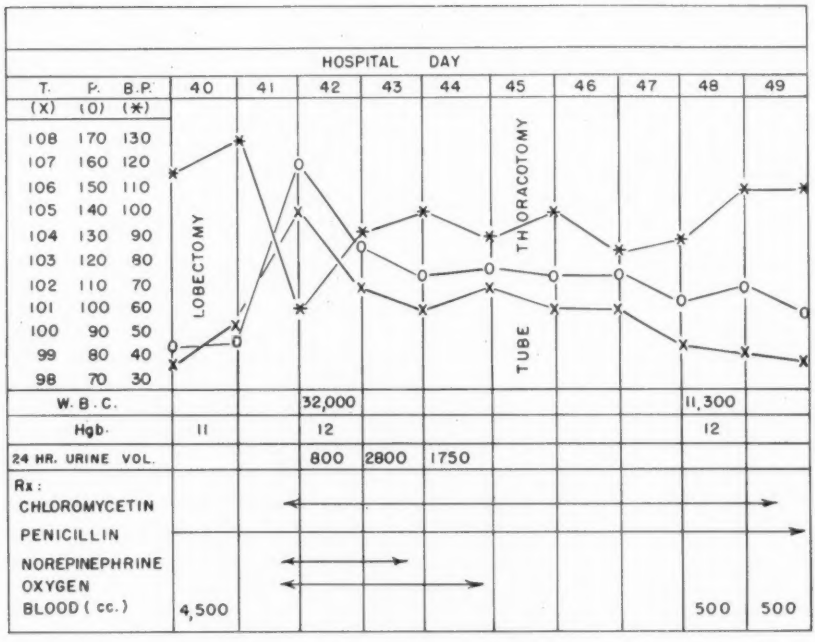

Fig. 3 (Case 3).—Course in a patient (C.) who developed pyothorax and septicemia produced by Aerobacter aerogenes and associated with marked circulatory collapse. Treatment included the administration of antibiotics, arterenol, and oxygen, blood transfusions, and tube thoracotomy.

February, 1953, and underwent lobectomy for bronchiectasis 10 months later, in December, 1953. Two days postoperatively he manifested evidence of septic shock, with the sudden rise of temperature to 107 F, an elevation of his pulse to 160, delirium, suppression of urinary output, and a fall in blood pressure to 60/0. His white blood cell count at the onset of shock was 32,000 per cubic millimeter.

He was given penicillin and chloramphenicol intravenously in large doses and arterenol by the same route at the rate of 8 cc. per 1000 cc. of 5% solution of dextrose in water. His blood pressure was maintained between 90 and 100 mm. Hg in this manner. A total volume of 800 cc. of urine was excreted during the first 24 hours after the onset of this therapy, and the volume was above 1000 cc. during the remainder of his illness.

After his response to supportive therapy a tube thoracotomy was done, and the patient then progressed to a complete recovery (Fig. 3).

Cultures of his blood and from the pleural space revealed repeatedly the presence of Aerobacter aerogenes, indicating that he had an associated septicemia. The hemolytic S. aureus, S. aureus var. albus, and a Pseudomonas were also cultured from the pleural space.

Case 4.—D., an 81-year-old woman, was admitted to the Cincinnati General Hospital on July 13, 1957. She was known to have an abdominal mass of four weeks' duration, complicated by a large-bowel obstruction. She was subjected to a sigmoidoscopic examination on July 28. Within 30 minutes of the completion of this procedure, the patient developed severe shock, manifested by a systolic blood pressure of 30 mm. Hg, a cold, clammy skin, urinary suppression, and a confused and apprehensive mental state. A diagnosis of ruptured abdominal abscess with septic shock was made, and the patient was immediately given arterenol, sodium penicillin G, and chloramphenicol by intravenous infusion. When the blood pressure was restored and the patient's condition improved, she was moved to the operating room on July 29 (12 hours later), where an exploratory laparotomy was performed under local anesthesia, and a ruptured abscess was found and drained.

At the completion of this procedure the concentration of arterenol necessary for maintenance of the systolic pressure near 80 mm. Hg was 40 cc. per 1000 cc. of 5% solution of dextrose in water. Even this was inadequate to maintain her pressure, and 100 mg. of hydrocortisone was then given intravenously, immediately followed by 50

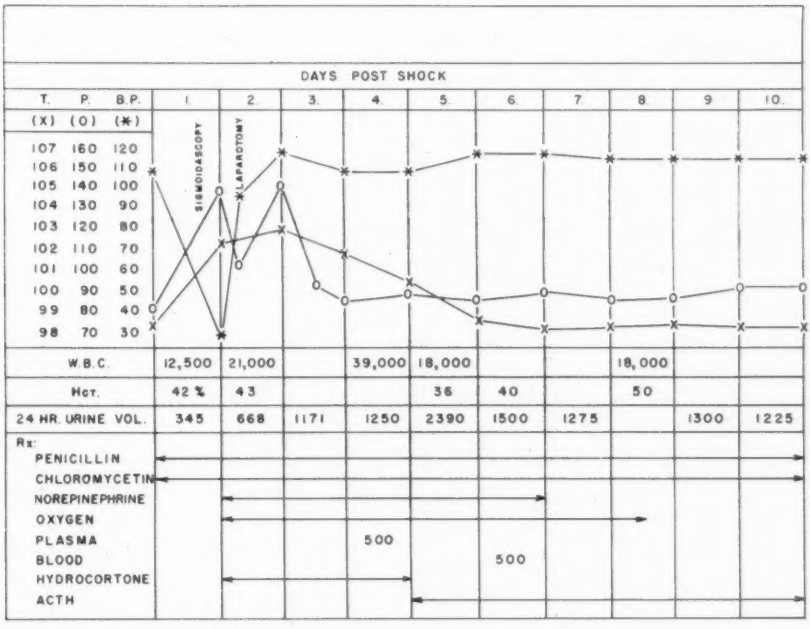

Fig. 4 (Case 4).—Chart showing the course of an 81-year-old white woman (D.) who developed circulatory collapse following rupture of an intra-abdominal abscess. Laparotomy and drainage of the ruptured abscess were performed after start of supportive treatment with arterenol, hydrocortisone, and antibiotics. Cultures of blood were repeatedly negative. Cultures from the abscess showed E. coli, P. vulgaris, and nonhemolytic Streptococcus.

mg. every six hours. Thus, it was possible to maintain the blood pressure and a urinary output of 25 cc. or more per hour for the first 24 hours. The white blood cell count, which rose suddenly to 21,000 at the onset of the shock, subsequently rose to 39,000 per cubic millimeter, indicative of the severity of the infection. After the third day the hydrocortisone was gradually reduced, and corticotropin was substituted for it for stimulation of the adrenal glands. The arterenol was discontinued on the fifth day, at which time a total of 1000 cc. of plasma and whole blood had been given. After an initial rise to 103 F, the temperature gradually fell to normal (Fig. 4). Cultures of the pus from the peritoneal cavity revealed Proteus mirabilis, Escherichia coli and a nonhemolytic Streptococcus. Repeated blood cultures were all reported as negative. The patient responded well to her treatment and made a complete recovery.

Comment

The results obtained in 16 patients in a series of 41 cases of septic shock are encouraging and indicative of the effectiveness of the basic principles of treatment which had been evolved. The importance of early recognition of these cases of septic shock in its treatment cannot be overemphasized. The chief factors responsible for failure of therapy were delay in diagnosis or failure to recognize the septic cause of the circulatory collapse when the process became terminal or irreversible.

If one keeps in mind the significance of the characteristic sharp curves of rising temperature, pulse rate, and white blood cell count and the coincident inverted curve of falling arterial pressure and urinary excretion, the early diagnosis of septic shock will be facilitated and its treatment more successful.

The observations that only 25% of these patients demonstrated any evidence of hemoconcentration supported our belief that large amounts of fluid replacement are not indicated and that they may be harmful in producing pulmonary edema if used in a

vain effort to restore the blood pressure. The evidence indicates, however, that fluids, particularly blood and plasma, should be given in moderation.

The intravenous infusion of arterenol in a 5% solution of dextrose in water appeared to be particularly useful when regulated to maintain a systolic blood pressure above 80 mm. Hg and a urinary output of 25 cc. or more per hour. By this method it was possible to maintain urinary function until the infection was brought under control and to permit the survival of the kidneys. It is interesting to note that arterenol was administered for periods up to 144 hours to patients who survived. Experience has confirmed the wisdom of infusing the arterenol through indwelling polyethylene tubing as a means of preventing local cutaneous gangrene. The use of the intravenous route for the administration of antibiotics in large doses appeared to be particularly efficacious in controlling the infection, but a period of two to seven or more days was required for this effect. This delay emphasized the importance of adequate supportive treatment to extend life until this antibiotic effect could be obtained.

Our early fears of permitting general dissemination of bacterial infection by cortisone therapy did not appear to be correct. The use of hydrocortisone in three patients appeared to be very valuable, and it is doubtful whether any of these patients would have survived without it. Additional experience is obviously needed.

Although it is generally better to treat a patient with a severe, uncontrolled infection conservatively and without operation, surgical intervention may be necesary in cases manifesting sudden vascular collapse during the course of a severe infection. It takes considerable knowledge, however, to determine which patients with septic shock require operative intervention, critical judgment to determine the time when this is feasible, and courage to perform an operation on such a critically ill patient who is being treated so vigorously by supportive drugs.

Summary

A plan of treatment for patients with septic shock had been evolved from observations made in a previous study of 93 fatal cases. This consisted of various supportive measures to sustain life and maintain urinary function until massive and effective antibiotic therapy could overcome the overwhelming infection. Surgical drainage or excision of the source of infection was done at a time when it was considered indicated and feasible. Emphasis was placed on the restricted infusion of blood and plasma, the administration of arterenol, the use of hydrocortisone when arterenol was inadequate, the administration of oxygen, and the intravenous injection of massive doses of the indicated antibiotic agents. The importance of early diagnosis and treatment was stressed in that it permitted successful treatment of this complication before the shock became terminal or irreversible.

In 41 cases seen during the past two years it has been possible to save 16 patients by this treatment. The methods used and the results obtained are described and illustrated with representative charts depicting the course of the patients with this complication.

The results obtained are encouraging, but considerable more knowledge and experience are needed for the successful management of this highly fatal condition.

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DISCUSSION

DR. GEORGE C. HENEGAR, Chicago: I have been interested in this problem for some time, especially when I was on the West Coast, where we were experimenting with the use of corticoids and corticotropin in this particular type of response in severe peritonitis. We reported on this about 18 months ago.

At that time it was our feeling that the use of hydrocortisone exerted something more than elevation of the blood pressure. For some reason or other, it blocked the toxic effect on the peripheral cells. Why, we didn't know; but at least that was the experimental effect, and we based our clinical work on those data.

By doing this it permitted one, if I may quote, "to buy time" for the antibiotics to take their effect; this antibiotic response is not immediate even if given intravenously.

We used intravenous hydrocortisone hemisuccinate as an immediate treatment and followed it with the long-acting corticoids intramuscularly and orally. One certainly cannot lean on any one particular therapeutic agent. We gave the patients all the supportive care that Dr. Altemeier outlined. I think this type of study is an important contribution to the care of the extremely sick patient.

DR. WILLIAM A. ALTEMEIER, Cincinnati: I would like to thank Dr. Henegar for his remarks, and indicate that we agree there is obvious improvement in the general condition of the patient with septic shock who is given cortisone therapy. Presumably this stems from the blocking of some of the toxic effects of the infection.

However, we feel that its major effects in these patients are to maintain a systolic blood pressure of 80 mm. Hg or more and to support the vital physiologic functions of the patient during the critical period until the antibacterial effects of treatment of the infection by massive doses of antibiotics with or without timed surgical intervention can be obtained.

It is interesting to note, however, that only 3 of the 16 patients who survived received cortisone, while 13 were treated with arterenol.

Surgical Complications in the Thorax of Staphylococcal Pneumonitis

DAVID HYDER WATKINS, M.D., Denver

Staphylococcic pneumonitis occurring in childhood has been recognized for many years, but until recently it has been regarded as a comparatively rare disease. This is indicated by the relatively small number of cases reported in the literature. Staphylococcal pneumonitis occurring as a complication of epidemic influenza has been known for a long time. The acute, fulminating, prostrating type occurring during the influenza pandemic of 1918 was described in the writings of Chickering and Park (1919).[1,2] At that time mortality rates of 80%-90% were reported. The staphylococcal pneumonitis occurring principally in infants carries a grave prognosis and usually occurs in sporadic form.[3] The gross mortality, in spite of antibiotic therapy, however, still remains high, with mortality figures in the range of 0 to 20%.

Relatively few cases of staphylococcal pneumonitis occurring in adults unassociated with major influenza epidemics were reported before 1950. In 1939 Heffon,[4] analyzing 3319 cases of lobar pneumonia, found only 6 that were considered staphylococcal. During more recent years, however, several large groups of cases have been reported. Out of 110 cases of pneumonia, Crofton (1951) [5] reported 10 cases which were considered to be staphylococcal. Grist (1952) [6] saw 10 cases of staphylococcal pneumonitis among 129 cases of pneumonia.

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From the Department of Surgery, University of Colorado and the Denver General Hospital.

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As antibiotics have been introduced for general use, antibiotic-resistant strains of staphylococci have appeared in those areas where each of the antibiotics has been used most extensively. This applies especially to large general hospitals. It has been shown that these organisms are predominantly endemic in hospitals, and it has been well demonstrated by Knight and his associates [7] that patients and personnel alike, upon entering the hospital environment, rapidly pick up the hospital staphylococci. It is reasonable to assume that pathogenic staphylococci are transmitted to patients shortly after their admission to the hospital by direct contact with bedding and, to a degree, with Staphylococcus carriers. A sudden outbreak of staphylococcal pneumonitis, terminating fatally in some instances, was recently reported by Ketcham and Brancato [8] which was attributable to a strain of hemolytic, coagulase-negative, drug-resistant Micrococcus pyogenes var. aureus, as well as coagulase-positive strains. While these organisms were regarded as serious enough infective agents in operative wound infections, they became dangerous, and rapidly lethal, in the respiratory tree of patients who had recently undergone major thoracic and abdominal operations.

The Staphylococcus may exhibit a number of properties in the bacteriologic laboratory, such as clotting fibrinogen, lysing rabbit and sheep cells, dissolving fibrin or mucin, and fermenting the carbohydrate mannite. However, experienced bacteriologists have doubted whether coagulase is an important factor in pathogenicity, since there is no evidence for in vivo clotting by coagulase. Protease and hyaluronidase do not appear

to be of significance as spreading factors in uncomplicated infections, but they may be of significance in synergistic double infections. Thus, the standard criterion of pathogenicity of staphylococcal isolates, the positive coagulase test, must be modified. The accuracy of the coagulase test may be questionable, for example, because of faulty plasma. Gram-stain smears of the freshly collected clinical material are primary aids in determining the significance of staphylococcal isolates. Whatever the results of the coagulase test, a properly collected clinical specimen showing intracellular cocci on smear and yielding in culture moderate to large numbers of staphylococci must be given serious consideration. It has been our experience that organisms found to be coagulase-negative have often been highly drug-resistant. While these strains are usually considered avirulent or of a low grade of virulence, if they possess a resistant antibiotic spectrum, they may become a serious threat to patients weakened by operation or other stress.

There are clear indications that age is a factor of great importance, especially within the pediatric age group. There is no doubt that staphylococcal pneumonitis is far commoner in infancy than in later childhood. About 10% of all empyema cases reported in children before the antibiotic era were due to the Staphylococcus. When infants less than one year of age are considered, this figure rises to 45%. The relative incidence of staphylococcal pneumonitis and empyema is seen to be an inverse function of age. Other forms of staphylococcal infection are not uncommon in early infancy. Postmortem examinations of infants dying suddenly and unexpectedly have revealed a significant number of instances in which staphylococci were recovered from the blood or from lung tissue.

The reasons for the striking age differential noted in cases of staphylococcal pneumonitis are of interest. Concentrations of serum γ-globulin and serum complement are low in early infancy. The circulating staphylococcal antitoxin levels decrease markedly during the first two to four months of life and remain low throughout the first year. Clinicians have long recommended programs designed to protect the premature, the newborn, and the young infant from contact with infective agents, such as the Staphylococcus.

Staphylococcal infection often directs its attack against damaged tissue and where local or general resistance is low. It is significant in this respect that in fibrocystic disease of the pancreas, where recurrent pulmonary infection is frequent, the Staphylococcus is responsible for the majority of cases and accounts for a high proportion of deaths (Anspach, 1947 [9]; Shwachman et al., 1949 [10]). Similar circumstances were present in 10 of the 18 cases reported by Hausmann and Karlish (1956).[11] Besides influenza, certain other virus infections predispose to staphylococcal pneumonitis. Among these are measles, chickenpox, and rubella. Other debilitating diseases which are associated with staphylococcal pneumonitis are amyotonia congenita, chronic gastroenteritis, epidermolysis bullosa, microcephaly, and rhabdomyosarcoma of the prostate. Such cases, present predominantly in children, occur in those who have been in the hospital for long periods before the onset of the pulmonary infection. This group emphasizes the frequency of staphylococcal infections in hospital patients and their commonly fatal nature in debilitated children.[12]

Epidemics of hemolytic staphylococcal infection in newborn nurseries have been reported in which fatal cases of staphylococcal pneumonitis develop. It is of the greatest interest to note that when these staphylococcal epidemics occurred, a similar organism was recovered from the purulent skin and subcutaneous lesions found in the nursery personnel. It is evident that sources of infection may be widespread within the hospital itself. Thus, the infant may be infected with resistant staphylococci, just as the adult hospital patient with, however, usually more disastrous results.

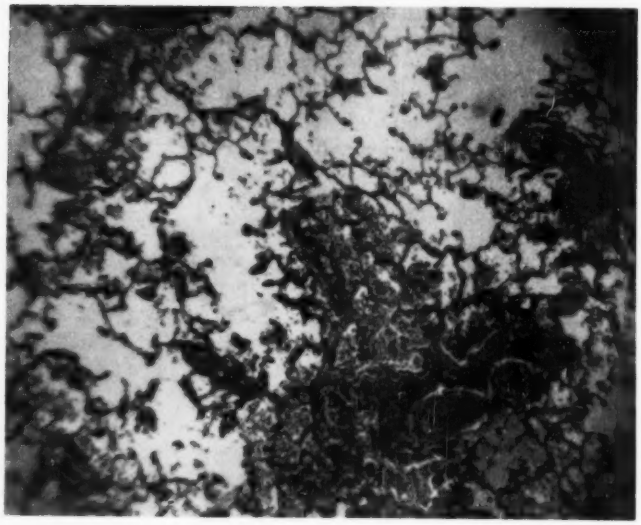


Fig. 1.—The early lesion of staphylococcal pneumonitis is focal alveolitis with congestion and edema of the alveolar septa and scattered focal areas of pulmonary edema. Scattered collections of polymorphonuclear leukocytes and macrophages are seen in the edema fluid.

Pathological Considerations

Staphylococcal infection of the lung may represent a primary bronchogenic respiratory infection, the organisms gaining entrance via the upper respiratory tract. Less commonly the infection is hematogenous, the primary site of infection being other than the lung. The earliest parenchymal change observed following the invasion of the lung by the staphylococci consists of diffuse, focal areas which present alveolar edema and congestion of alveolar capillaries (Fig. 1). A more advanced stage is characterized by an exudate, again focally distributed, of polymorphonuclear leukocytes mixed with varying numbers of large macrophages. In some cases the pneumonitis is hemorrhagic, with large numbers of erythrocytes mingling with leukocytes in edema fluid. Masses of cocci are frequently seen in the centers of areas of marked change. There is a prominent and characteristic tendency to early

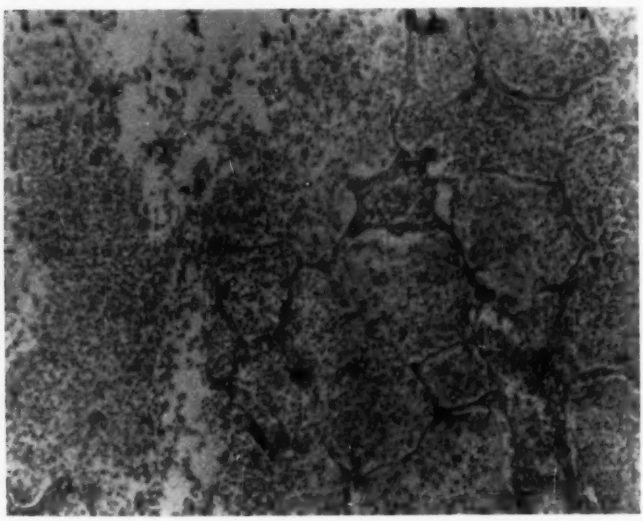


Fig. 2.—The next stage is an increase in the number of polymorphonuclear leukocytes in the exudate, lysis of interalveolar septa, and thrombosis of small pulmonary veins.

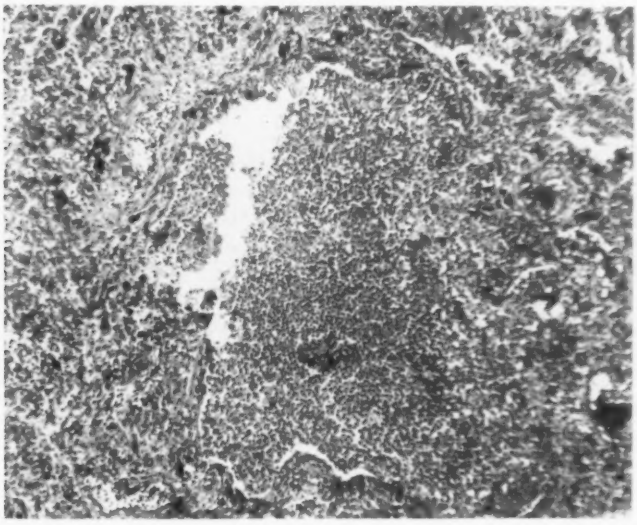


Fig. 3.—Extension of the inflammatory process to produce a microabscess, with masses of cocci in its center, a purulent exudate, young granulation tissue surrounding the pus, and thrombosed small pulmonary veins.

necrosis of the alveolar walls and of the cells of the exudate (Fig. 2). Gradations are seen between zones of necrotizing pneumonitis and acute microabscess formation. These microabscesses usually contain masses of cocci, in addition to degenerating polymorphonuclear leukocytes, remnants of the alveolar framework, and pale-staining granular debris. Occasionally, there is an additional hemorrhagic content. In some instances, bronchioles apparently communicate directly with the microabscesses. Frequently, bronchioles and large bronchi are situated in contiguity with segments of the abscess wall (Fig. 3). Occasionally granulation tissue with proliferating fibroblasts is observed in the boundary zone of the microabscess, but no evidence of collagenous scar appears. Sometimes thin pulmonary septa are incorporated into the wall of the abscess.

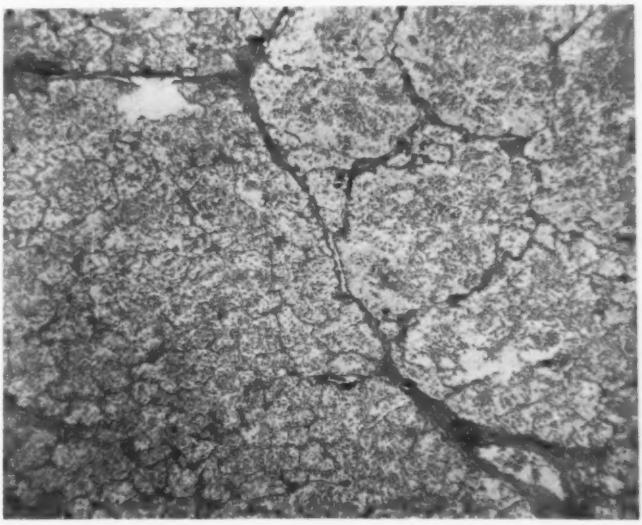


Fig. 4.—Confluence of the diffuse focal microabscesses to produce areas of pneumonitis, which may involve larger and larger segments of the pulmonary anatomy until a lobar pneumonia is produced.

There is a distinct tendency for these microabscesses to become confluent and form larger, consolidated abscess cavities. These abscesses tend to vary in size and to be complex and ramified. Clusters may be seen about the bronchioles. Other findings may include recent thrombosis of pulmonary veins, edema and cellulitis of pulmonary septa, and, occasionally, fibrin thrombi in septal lymphatics (Fig. 4). In areas of pulmonary tissue bordering the zones of pneumonitis and abscess formation the alveoli, and the bronchioles, frequently show the changes characteristic of lipid pneumonitis, with moderate numbers of foamy macrophages. For the most part, however, the univolved pulmonary tissue shows only marked atelectasis.

Pleural surfaces are involved in all cases. Early involvement is characterized by congestion of the small blood vessels and dilatation of lymphatics in the subpleural fibrous tissue, with associated interstitial edema and an infiltrate of mononuclear and polymorphonuclear inflammatory cells. There is loss of the pleural mesothelium with a delicate fibrinous deposit on the pleural surface. Usually, however, a much more advanced inflammatory process is seen, the pleural surfaces being covered by thick, dense fibrin layers, in which degenerated polymorphonuclear leukocytes are present. In a few areas granulation tissue gives evidence of early attempts at organization.

Pulmonary abscesses of varying size may be subpleural in location and may rupture into the pleural space to cause empyema (Fig. 5). If such an abscess has a small bronchial communication and ruptures into the pleural space, pyopneumothorax results.[13] The empyema or pyopneumothorax almost always occurs early in the course of the disease, giving insufficient time for adhesive pleuritis to form. An abscess may break into and evacuate its contents through a bronchiole; the result is a cyst-like space. The wall of that particular bronchiole which leads into this space is edematous and inflamed, allowing air to ingress but not to egress. This produces a check-valve type of mechanism, which, together with restricted collateral ventilation and normal expiratory bronchial constriction, causes enlargement of the "cyst-like" space, displacing adjacent pulmonary tissue. This space is commonly referred to as a pneumatocele. If the pneumatocele is located subpleurally, it may rupture into the pleural space to produce a tension pneumothorax. When the pathologic bronchial changes subside and the check-

Fig. 5.—Subpleural pneumonic focus undergoing organization. The marked fibrinous pleural exudate, which is also organizing, is well seen. It is thought that in this case the area represents the site of perforation of a pneumonic focus which produced a pyopneumothorax.

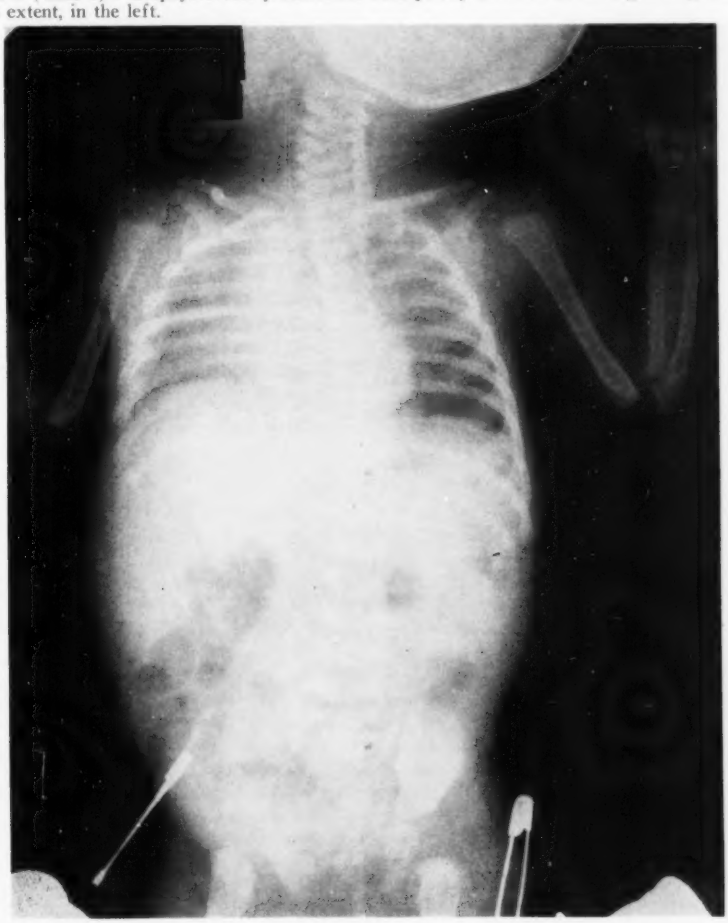
valve mechanism relents, air in the pneumatocele is absorbed. Pneumatocele and emphysema are common complications in this disease, and, although they are usually transient and quite reversible, this is not always the case. Sometimes a pneumatocele may require a period of six to nine months before it resolves. Spontaneous pneumothorax can occur at any time, and when the patient is clinically doing very well, even late in convalescence.[14]

Illustrative Cases

CASE 1.—A., a 3-month-old, premature female infant of Spanish-American origin, was admitted for the first time to the Denver General Hospital on Feb. 13, 1957, for bronchopneumonia. The present illness had started on Feb. 6, with cough, fever, nasal discharge, and vomiting. Three days before admission the baby had developed diarrhea. The cough did not improve; fever continued, and the baby kept on vomiting a considerable amount of material every day. For two days before admission the baby had refused most of her formula. The birth weight was 4 lb. 8½ oz. (2055 gm.). No oxygen or incubator was necessary. She had been in the pediatric clinic because of poor suckling, and her appetite had always been poor. She did not turn on her abdomen and did not hold her head well.

Physical examination showed her weight to be 3805 gm., temperature 39.6 C (103.3 F), respiratory rate 40 to 60 per minute. She was pale, small,

Fig. 6 (Case 1).—Staphylococcal pneumonitis with patchy densities in the right lung and, to a less extent, in the left.



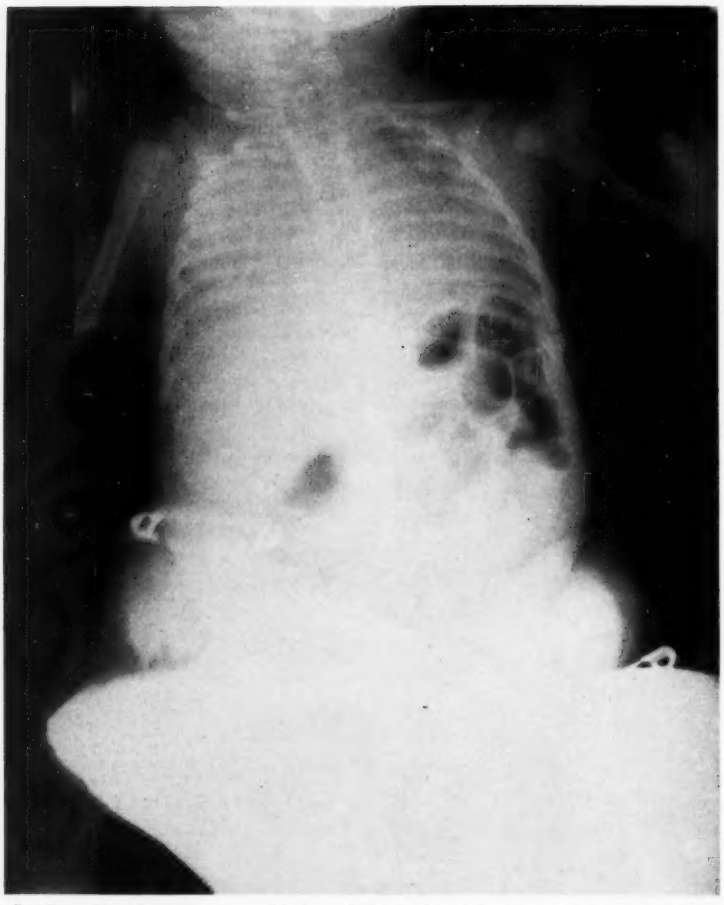


Fig. 7 (Case 1).—Apparent consolidation of the entire right lung and presence of scattered patchy infiltrates in the left lung field.

poorly nourished, and poorly hydrated, and showed active, rapid breathing. The skin had rather poor turgor. An erythematous rash on the back, with three or four prominent bluish areas, were present on the back and shoulders. Red confluent spots, which bled under pressure, were present over the left forearm. No other skin lesions were found. The lymph nodes were not remarkable. There was perioral lividity. The anterior fontanel was depressed; the sutures were not enlarged, and the posterior fontanel was closed. The tympanic membranes were pale, and there was no bulging of those membranes. The nose was clear. The mouth and throat showed fairly dry membranes with little saliva. The patient was breathing rapidly. The expiratory phase was not prolonged. There were good breath sounds bilaterally. There was questionable dullness on the superior portion of the right chest. The left chest was dull posteriorly only. No rales were heard. The heart was rapid and regular, with good sounds and no murmurs. The abdomen was not distended, and no masses were felt. The spleen was not palpable, nor was the liver enlarged. Stools were normal. The child exhibited good activity, but she was irritable and anxious. Spinal fluid was crystal clear, with 690 mg. of chloride, 20 mg. of protein, and 100 mg. of sugar, per 100 cc. The hemoglobin was 12.5 gm. %. Total leukocyte count was 28,600, with 64% polymorphonuclear cells. Urinalysis showed slight albuminuria. Roentgenograms of the chest (Fig. 6) showed patchy densities in the right lung and, to a less extent, in the left.

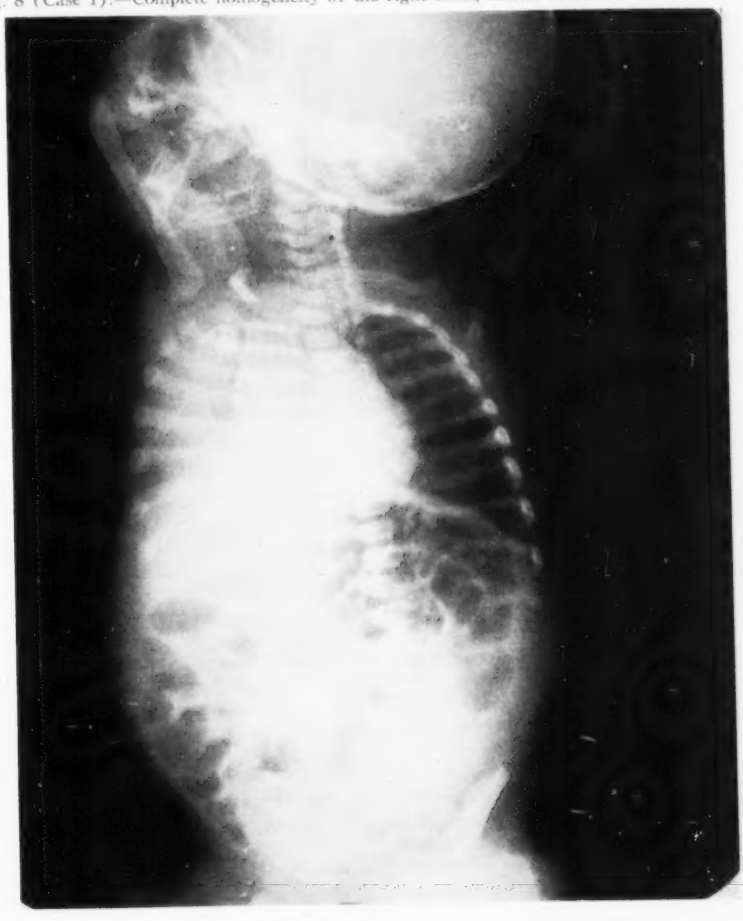
On Feb. 16, nose and throat cultures were reported as overgrown with Proteus. She had now been on penicillin and streptomycin therapy for

three days. The temperature seemed to respond well. At this time she had circumoral cyanosis and cyanosis of the lips. She was markedly irritable, with tachypnea of 50 to 60 per minute. On percussion the right chest was entirely dull; the breath sounds were diminished on the right anteriorly and posteriorly, and the voice transmitted well. A few crepitant rales were present on both sides. Note was made that the pneumonia in the right lung was inconspicuous on admission. At this time, three days later, the entire right lung appeared to be consolidated, and scattered, patchy infiltrates were present in the left lung field (Fig. 7). Therapy was switched from penicillin and streptomycin to penicillin and chloramphenicol, with continuation of the oxygen tent and detergents.

On Feb. 17 the patient was digitalized. On Feb. 18 the baby was taking sufficient fluids but started to have diarrhea, which was thought to be due to the influence of antibiotics and severe infection. A roentgenogram showed complete homogeneity of the right chest, most likely a combination of effusion and consolidation (Fig. 8). On Feb. 21, there was no change in the physical signs, and the patient was afebrile. However, she continued to be cyanotic when taken out of the oxygen tent. The liver was 3 fingerbreadths below the right costal margin.

On Feb. 21 the patient was seen by the surgical service. Thoracentesis was performed, with the removal of 70 cc. of thick, greenish pus, and intercostal water-seal drainage was instituted by a No. 20 mushroom catheter inserted into the eighth interspace in the right posterior axillary line under local anesthesia. A considerable amount of thick pus was exuded from the pleural cavity.

Fig. 8 (Case 1).—Complete homogeneity of the right chest, due to effusion and consolidation.



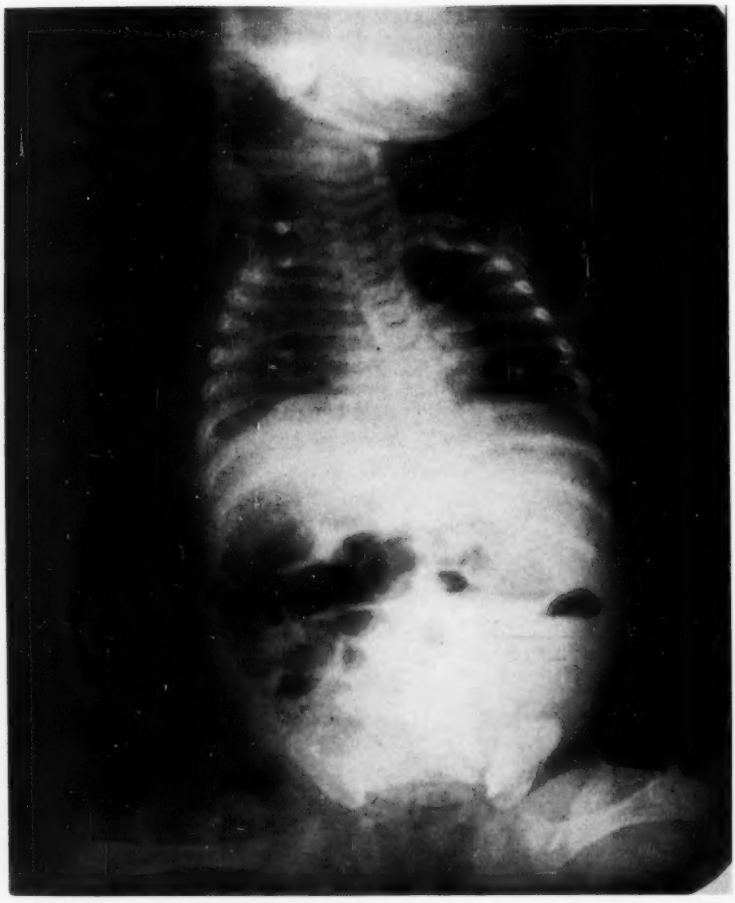


Fig. 9 (Case 1).—Residual pneumonic infiltrates in the right lung and some residual pleural effusion in the lowermost part of the major fissure on the right.

On Feb. 22 the condition was improved in that the child's temperature had decreased to normal. Cultures of the empyema fluid showed S. aureus, coagulase-positive, sensitive to chloramphenicol, bacitracin, novobiocin, and nitrofurazone. Roentgenograms showed pneumonic infiltrates in the right lung and some residual pleural effusion in the lowermost part of the major fissure on the right (Figs. 9 and 10).

On Feb. 24 the baby was improving. Breath sounds were heard over the entire right chest. On March 1 breath sounds on the right side were decreased, and by March 4 it was noted that the patient's condition had greatly worsened during the past two days and she had a spiking fever, with elevations to 101.3 F. She required dropper feedings because of weakness. The infant was pale and lethargic, and respirations had increased to 80 a minute and were shallow but regular. The abdomen had become protuberant, with normal bowel sounds, and the liver was 1 finger-breadth below the costal margin. Roentgenograms showed marked clearing of the right lung at this time and no residual pleural effusion. Marked abdominal distention was present, with gas in many intestinal loops (Fig. 11).

On March 5 it was noted that the patient had developed an ileus, with marked distention and decreased breath sounds bilaterally. Later that morning, after fluid and mineral replacement, the child was afebrile and looked better. However, the abdomen continued to be very distended, but good breath sounds were present bilaterally.

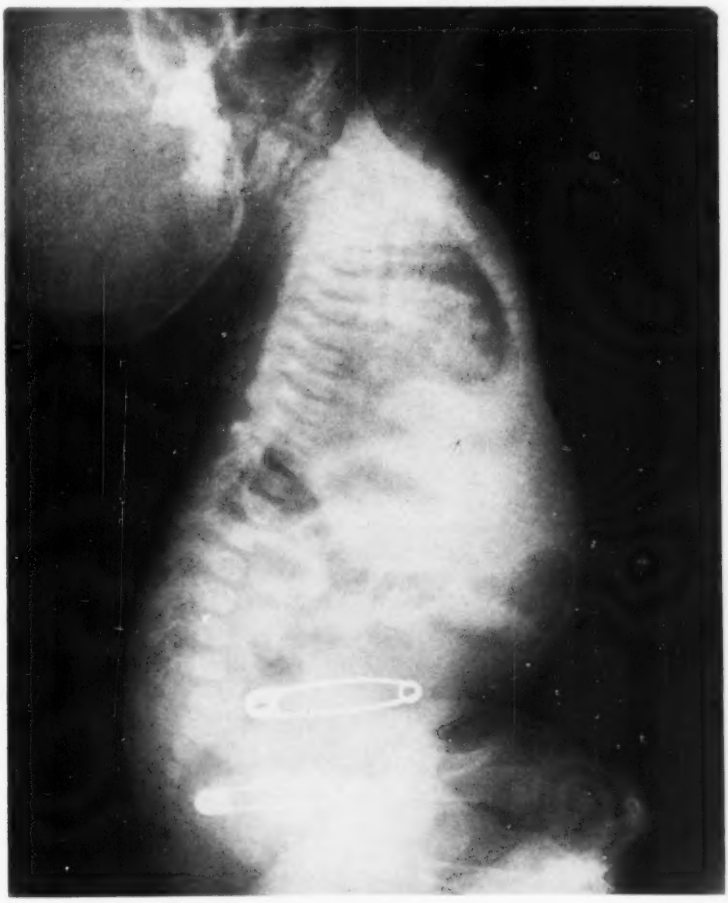
That afternoon at 3 p. m. the abdomen was massively distended and tympanitic. No breath sounds were heard. At that time our pediatric

consultant made this note on the chart: "I am struck with the sequence of fever, leukocytosis, then distention and vomiting; these suggest peritonitis. The x-ray does not rule out volvulus, for the large loops of the bowel, which superficially look like transverse and descending colon, may well be small bowel. Peritonitis and volvulus will require change in antibiotics and surgical exploration." The infant's course was progressively downhill, and she died March 5. Roentgenogram (Fig. 12) showed the marked degree of ileus which was verified at autopsy.

This case illustrates the predisposing influence of prematurity, the tendency of the disease to involve the pleura, and the prompt amelioration of the empyema by closed intercostal drainage. In spite of the fact that the pleural complication was controlled, the child died of progressive pulmonary lesions. Marked abdominal distention was characteristic of the terminal stages of the disease.

CASE 2.—B., a male child, was born on Dec. 24, 1956, and represented a full-term pregnancy. He was seen at the Denver General Hospital in the pediatric clinic on Jan. 18, 1957, with a conjunctivitis which had involved the left eye for two weeks and had then extended to the right eye several days before observation here. He also had developed small pustules around the umbilicus and on his thighs since dismissal from the hospital. Examination at that time showed scattered pustules on the skin and marked bilateral conjunctivitis and blepharitis. On Jan. 25, 1957, he was referred to the pediatric clinic because of an illness diagnosed as pneumonia by the family physician. At that time the child had had no

Fig. 10 (Case 1).—Lateral view corresponding to Figure 9.



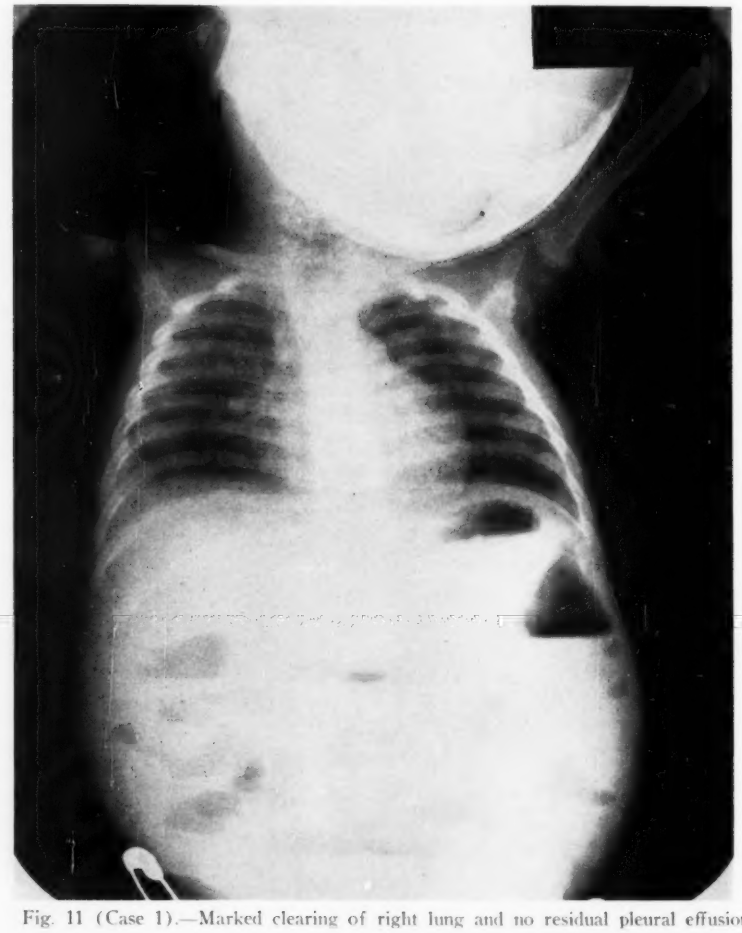


Fig. 11 (Case 1).—Marked clearing of right lung and no residual pleural effusion.

respiratory distress, and physical examination of the chest showed only a few scattered rhonchi. A chest roentgenogram at this time was negative.

The child was seen again on March 1, at which time he was 8 weeks old. The chief complaints at this time were cyanosis and distention. Two weeks prior to admission he developed a bilateral ear infection, in addition to the preceding conjunctivitis; both ears had been draining for the past week. Two days prior to admission the patient's abdomen became distended, and he failed to have bowel movements. In addition, he had been breathing with grunting respiration and vomited frequently.

Physical examination showed marked dyspnea, with wet rales bilaterally and diminished breath sounds in the right chest. The abdomen was markedly distended. Bowel sounds were high-pitched. The patient had a large umbilical hernia. The child was admitted to the surgical service, where a right pneumothorax with bilateral pneumonitis was demonstrated by the roentgenogram (Fig. 13). Aspiration was done on the right thorax, with removal of 40 cc. of pus, from which a coagulase-positive, hemolytic S. aureus was cultured. It was felt that the abdominal distention was most likely accounted for on the basis of ileus, and the patient was treated by nasogastric intubation, parenteral administration of fluids, a humidified tent, and frequent suction of the tracheobronchial tree. Treatment was started with tetracycline and novobiocin, but the course was steadily downhill, and the infant died that same evening.

Autopsy disclosed extensive lobar pneumonia involving the entire right lung, with empyema, pneu-

mothorax, and total collapse of the right lung. A marked ileus was present.

The importance of avoiding exposure of the newborn infant to the Staphylococcus is illustrated here. The surface infections apparently were responsible for the bacteremia, which produced a metastatic pneumonitis. The pneumonitis, once established, followed a well-known pattern.

CASE 3.—C., an 8-month-old boy, was brought to the Denver General Hospital by his mother on Jan. 12, 1957, because of poor general condition, weakness of the legs, and poor appetite. The child had been the product of a normal pregnancy and weighed 6½ lb. (2736 gm.) at birth. He had never been hospitalized, nor had he been seriously ill. Two weeks prior to admission he started teething and had been in poor health since then. One week before admission he refused food and began coughing. He had no fever until the day prior to admission.

Physical examination showed a weight of 5850 gm., a respiratory rate of 60 per minute, temperature 37.3 C (99.1 F), and pulse 120 per minute. The patient was seen to be a small, pale, grayish, chronically and acutely ill-looking 8-month-old male child in fairly severe respiratory distress, malnourished, and moderately dehydrated. The skin showed poor turgor with very poor subcutaneous tissue. The arms were very thin; the hands were cold and appeared very pale. The lower limbs allowed passive motion; apparently they were not painful. However, the child showed no active movements of the right leg, which was completely flaccid. Both lower extremities were dif-

Fig. 12 (Case 1).—Supine view of abdomen showing marked preterminal ileus.

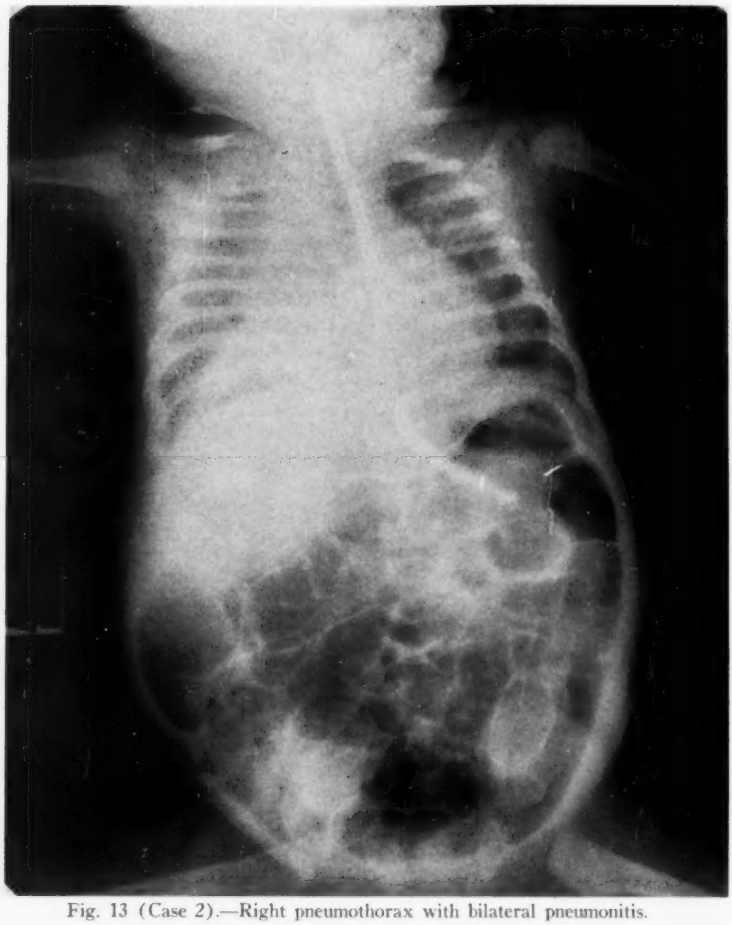


Fig. 13 (Case 2).—Right pneumothorax with bilateral pneumonitis.

fusely edematous. Nose, throat, and ears were negative. Respiratory rate was 60 per minute, and respiratory movements were symmetrical. Slight inspiratory intercostal retraction was observed. The left hemithorax was entirely dull anteriorly and posteriorly, and no breath sounds could be heard over this area. The right hemithorax showed fair breath sounds, with a few crepitant rales heard at the apex on inspiration, and was normally resonant anteriorly and posteriorly. The heart was negative, but the femoral pulses were not palpable on either side. The abdomen was slightly distended; the liver edge was felt 3 cm. below the right costal margin. The inferior pole of the spleen was palpable on inspiration 4 cm. below the left costal margin.

Neurological examination disclosed an anxious-looking baby, with a weak and monotonous cry and labored respiration, who lay on his back. Muscle tone was weak throughout. No abnormal movements were observed. The neck and back were supple. The anterior fontanel was slightly depressed. The deep tendon reflexes were weak but present bilaterally in the upper limbs; they were absent, however, in the right lower limb. The ocular fundi and movements were normal. Sensitivity was much decreased in the right foot, leg, and thigh; it seemed to be normal in the left lower extremity.

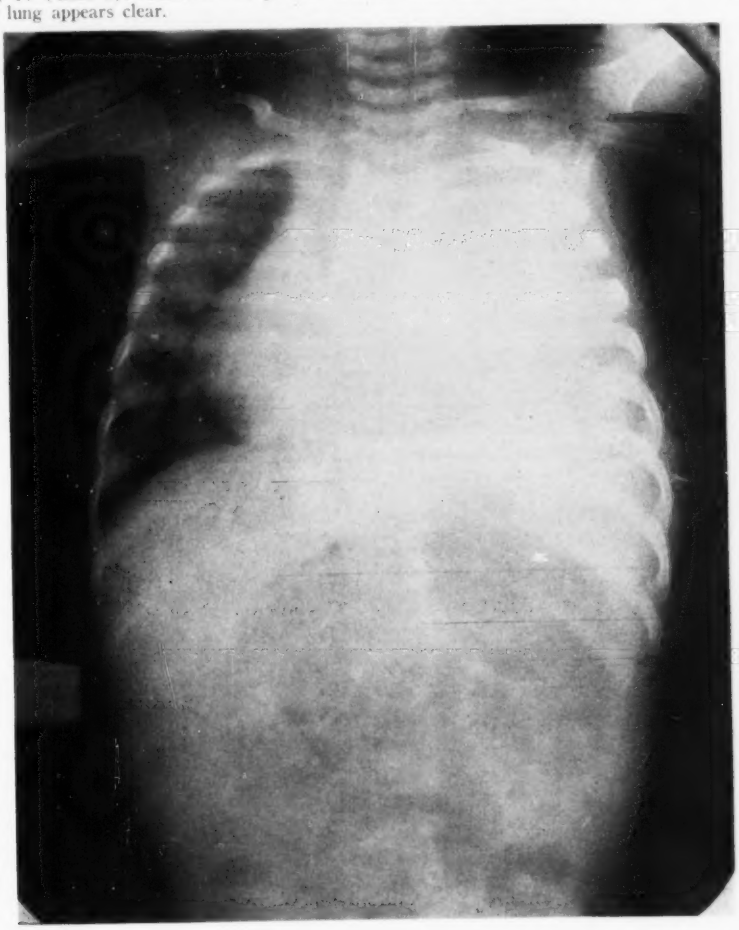
Hemoglobin was 13.2 gm. per 100 cc.; total leukocytes numbered 11,850 per cubic millimeter, with 36% polymorphonuclear leukocytes. Urinalysis was negative. Examination of the spinal fluid showed it to be normal. The roentgenogram (Fig. 14) showed a marked amount of pleural effusion on the left, displacing the heart to the right. The right lung appeared clear.

Thoracentesis was performed. From the left pleural cavity 50 cc. of foul-smelling pus was obtained. On culture, a coagulase-positive, hemolytic S. aureus was demonstrated. The organism was proved sensitive to erythromycin, novobiocin, and chloramphenicol. The patient was initially started on treatment with penicillin, chloramphenicol (Chloromycetin), and erythromycin. Intercostal closed drainage tubes were placed by closed thoracotomy anteriorly and posteriorly, two No. 16 catheters being inserted in the left chest. Four hundred cubic centimeters of pus was removed under pressure.

Neurosurgical consultation raised the question of an epidural abscess contiguous with the empyema, although this diagnosis was incompatible with the presence of severer weakness on the right in the absence of any sensory changes in this area. An intravenous pyelogram appeared normal. The patient continued to be treated by chloramphenicol, streptomycin, and penicillin. Immune γ-globulin was also given.

The patient continued to have a septic, febrile course. On Jan. 15 the fluid previously described was seen to have almost completely disappeared (Fig. 15). A pneumothorax was present. The film of Jan. 18 (Fig. 16) shows the intercostal drainage tubes in the left hemithorax, but the lung has not completely expanded. On Jan. 23 a fluctuant swelling was noted in the left buttock, and rectal examination revealed a fluctuant pelvic mass. The abscess on the left buttock was incised and drained. On Jan. 24, both chest tubes were removed, and the left lung appeared completely

Fig. 14 (Case 3).—Marked left pleural effusion with displacement of heart to the right. Right lung appears clear.



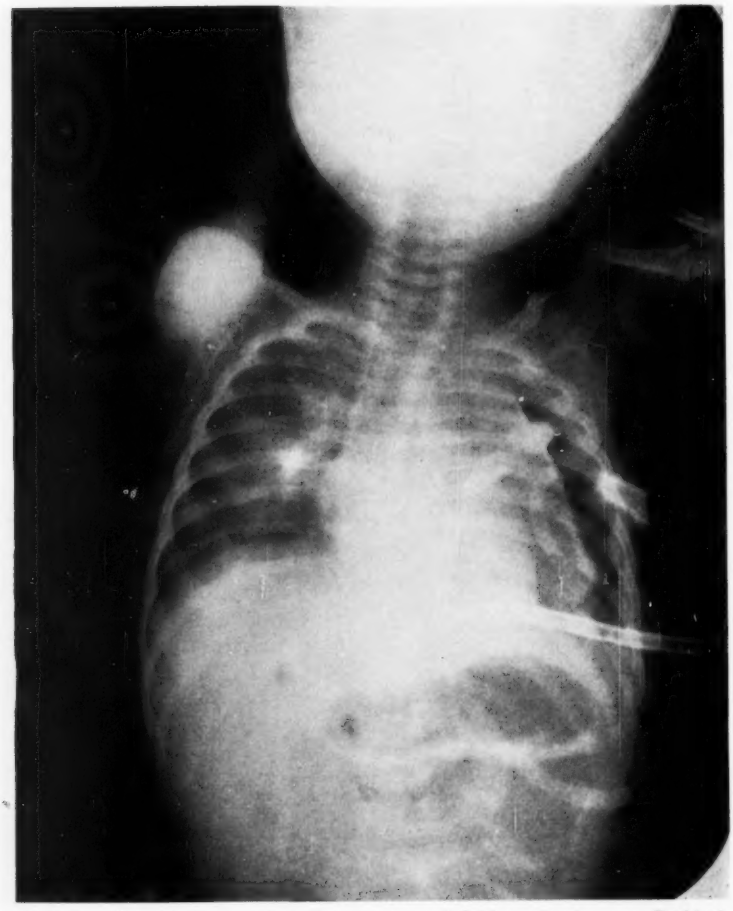


Fig. 15 (Case 3).—Almost complete disappearance of fluid previously seen. Residual pneumothorax is present. Drainage tubes are in position.

expanded. The patient developed diarrhea at this time, and Pseudomonas was cultured from the stool. The infant was then placed on polymyxin orally. On Jan. 28 roentgenograms (Fig. 17) showed a large empyema cavity with an air fluid level on the left. The lung was almost completely obscured by pleural reaction. There was apparent shift of the mediastinum toward the right.

On Jan. 28, the left chest was tapped posteriorly, and 80 cc. of pus was removed. On Feb. 3 a No. 14 rubber catheter was inserted into the left second interspace in the midclavicular line, with decompression of tension pneumothorax, and 30 cc. of pus was obtained. On Feb. 11 the chest tube was changed, and a No. 16 Pezzer tube was placed in the left second interspace, with good fluctuation.

On Feb. 13, a left thoracotomy was performed, and a thick peel was removed from the parietal and visceral pleurae of a large empyema cavity. On Feb. 18, the penicillin and erythromycin were stopped, and treatment was continued on chloramphenicol and oxytetracycline. The temperature was continuing to spike to 39.5 C (103.1 F) daily, but the patient seemed to be improving. He died suddenly on Feb. 20.

The postmortem examination showed septicemia due to a coagulase-positive S. aureus with diffuse left pneumonitis and atelectasis, left empyema, pyelonephritis with multiple abscesses, focal cholangitis with microabscesses, and right pulmonary emphysema and edema. The blood cultures obtained postmortem were positive for staphylococci.

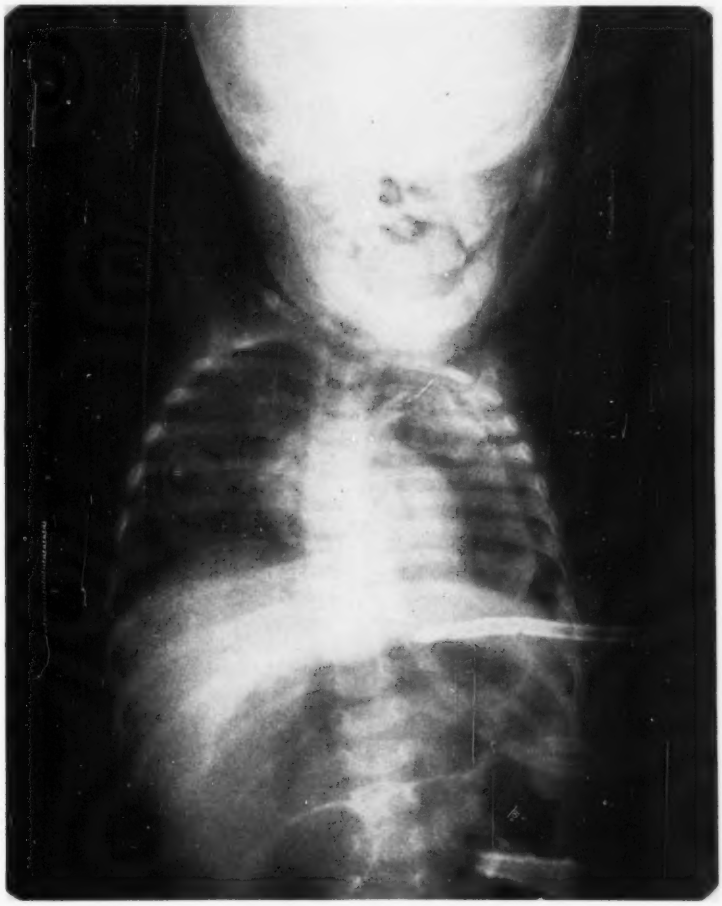
The patient here was suffering from an undiagnosed chronic neurologic disorder

which had produced paralysis of the right leg. The stress incident to teething had been responsible for the onset of the Staphylococcus pneumonitis. The tendency to recurrence of the pleural complications and the lateness of their development are shown. In spite of in vivo sensitivities to several antibiotics, the course of the disease was little influenced.

CASE 4.—D., an 85-year-old white man, was in good health until eight days prior to admission, on Dec. 11, 1957, when he developed cough, fever, malaise, and sputum. Three days prior to admission the patient had an increase in productive cough, a temperature of 100 F, and dyspnea. He had no prior history of pulmonary disease. On physical examination, the pulse was 90, blood pressure 90/50, respiration 22, and temperature 37 C (98.6 F). The anteroposterior diameter of the chest was increased, and the range of chest motion was much diminished. Breath sounds and decreased fremitus over the right base posteriorly were present, with an occasional expiratory wheeze. Laboratory examination on admission showed the hemoglobin to be 15.3 gm. per 100 cc., and total leukocytes 7100, with 53% polymorphonuclear cells. The urine was loaded with bacteria and numerous white cells. Hematocrit was 46%.

A right thoracentesis, with removal of 800 cc. of clear, straw-colored fluid, was carried out. The following day, right thoracentesis was repeated, and 1400 cc. of clear, straw-colored fluid was removed. The venous pressure at this time was 8 cm. of water. The following day the patient was found to have a pneumothorax at the site of thoracentesis,

Fig. 16 (Case 3).—Increasing but not yet complete expansion of left lung.



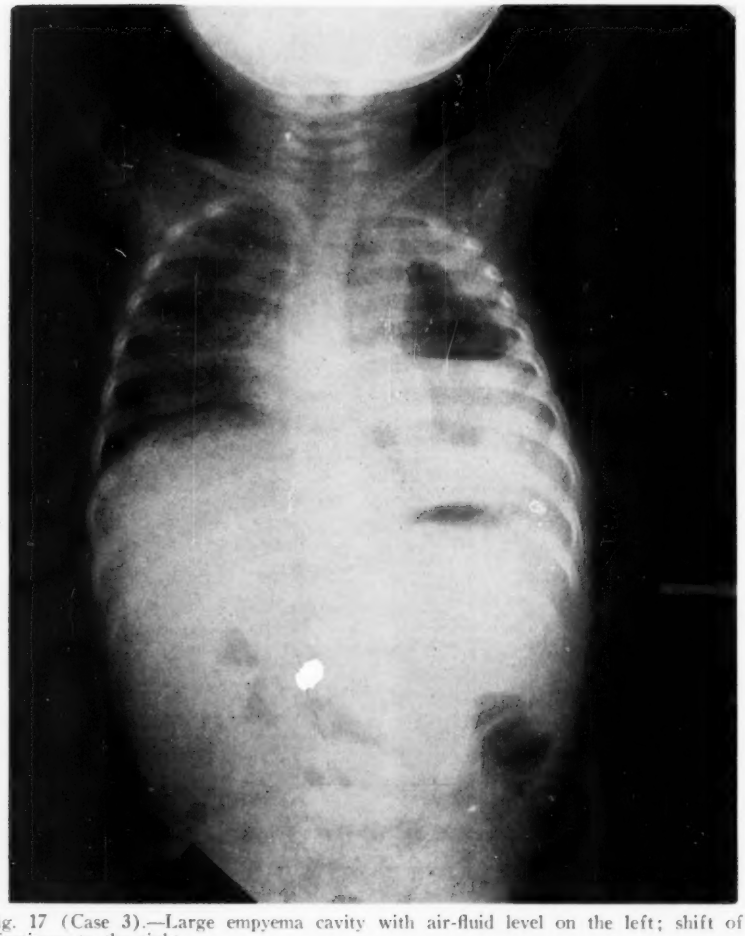


Fig. 17 (Case 3).—Large empyema cavity with air-fluid level on the left; shift of the mediastinum to the right.

which had progressed to involve collapse of the middle and lower lobes on the right (Fig. 18). A chest tube was placed in the second right interspace, with expulsion of much air and some fluid. By the following day the lung had completely reexpanded. That evening the blood pressure suddenly dropped and the temperature rose to 38.6 C (101.5 F). Examination showed the patient to be stuporous and incoherent. The blood pressure was 90 systolic, with a pulse rate of 84 and a respiratory rate of 30, a minute. Further examination disclosed a pneumothorax on the left side; and 600 cc. of air was aspirated, and an intercostal tube was inserted in the left fourth interspace. A roentgenogram taken immediately afterward showed reexpansion of the left lung with slight residual pneumothorax at the left base. Infiltrative densities were present throughout both lungs, more marked on the right (Fig. 19). The patient was given intravenous hydrocortisone and was continued on erythromycin, chloramphenicol, and penicillin. He held his own during the next few days, and on Dec. 18 bronchoscopy was carried out because of recurring atelectasis of the lower and middle lobes of the right lung. Thick mucous plugs in the right lower lobe and in the right-middle-lobe bronchi were removed. His postoperative condition was good. Following this procedure the chest films showed better expansion of the lungs. On Dec. 20, a tracheostomy was done because of his difficulty in coughing, and a large quantity of mucoid secretion was removed from the tracheobronchial tree. On Dec. 23 both chest tubes were removed. The patient continued to be

confused and to have a very low blood pressure. His course was progressively worse, and he died on Dec. 27.

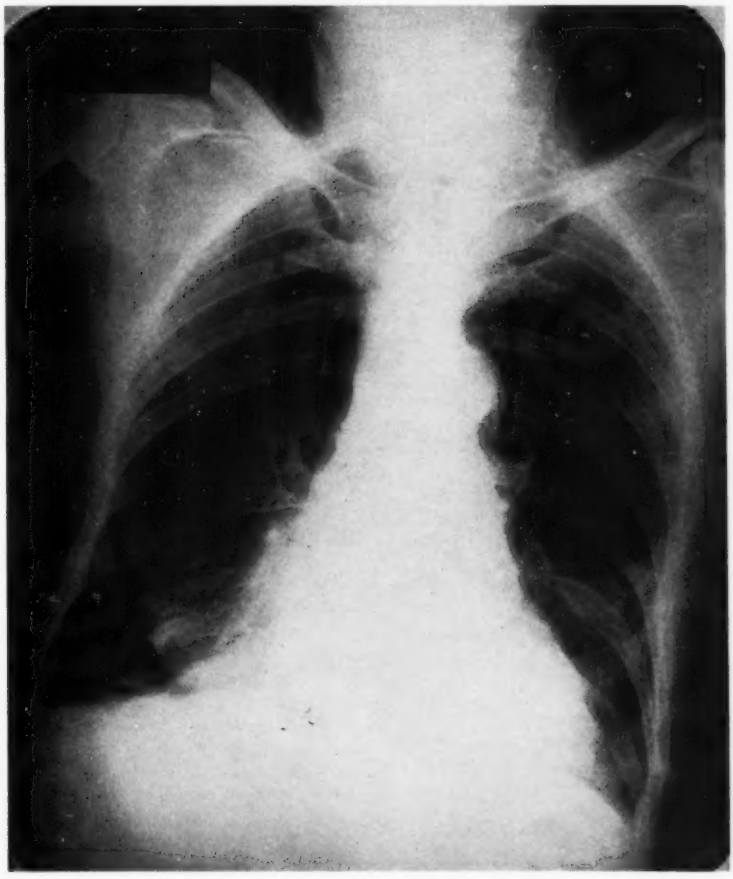
Autopsy disclosed that the patient had bilateral diffuse acute and chronic pneumonitis due to hemolytic coagulase-positive S. aureus, severe emphysema, acute gastric, and duodenal ulcers.

The pneumonitis, with its complicating bilateral pneumothorax, occurred here apparently with no predisposing illness but merely with advanced age. Antibiotics and supportive therapy did nothing to alter the course of the disease.

CASE 5.—E., a 7½-year-old Negro boy, had been in apparent good health until four days prior to admission, on Aug. 22, when he was struck on the nose with a football. Three days prior to admission the nose began to swell and become painful. One day before admission the patient had developed a fever and had been disoriented. He had had marked anorexia for the three days preceding admission. On the day of admission he complained of severe frontal headache and epistaxis. In 1953 he had developed a slight heart murmur, which was attributed to rheumatic fever.

Physical examination showed the pulse to be 100 a minute, temperature 39 C (102.2 F), and blood pressure 110/70. He appeared to be in moderately acute distress, thrashing about in bed and appearing acutely ill. There was proptosis of both eyes, more marked on the right. Ocular fundi appeared normal. Examination of the nose showed swelling and tenderness of the entire nose and crusting of blood on the septum. The neck resisted flexion, but the chin could be placed on

Fig. 18 (Case 4).—Pneumothorax producing collapse of right middle and lower lobes. Scattered infiltrative densities in right lung.



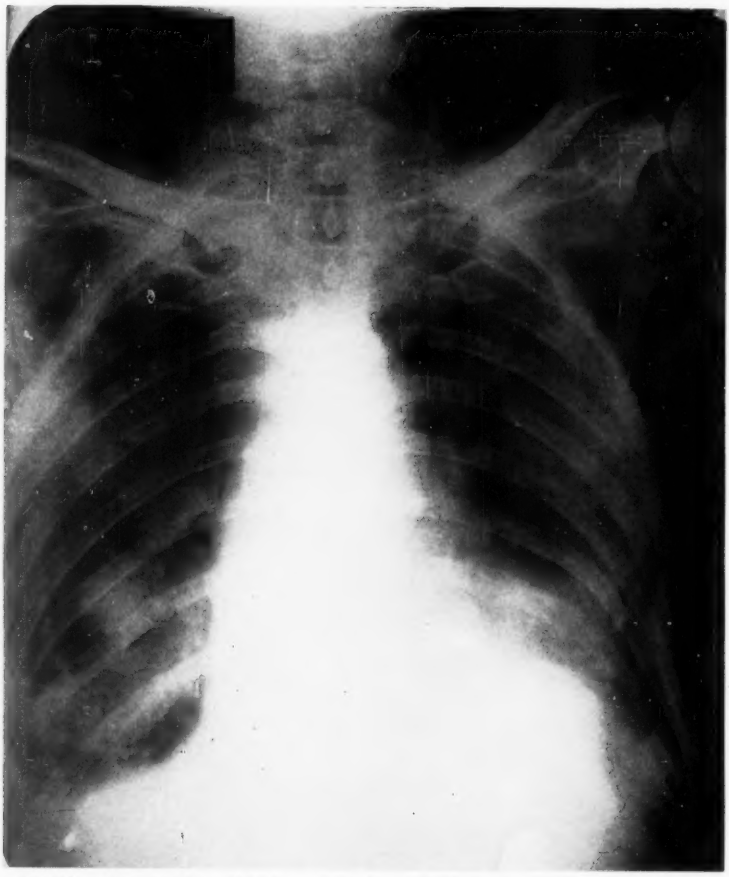


Fig. 19 (Case 4).—Slight residual pneumothorax following tension pneumothorax on left. Infiltrative densities present throughout both lungs, more marked on the right.

the chest. The patient was disoriented, delirious, and semicomatose.

Admission urinalysis on Aug. 23 showed 4+ albumin and positive tests for acetone; there were 20 to 30 red cells per high-power field. Examination of the blood showed a hemoglobin of 12.9 gm. % and a leukocyte count of 15,000, with 66% polymorphonuclear cells. His hematocrit was 37%. Spinal fluid on admission showed 443 leukocytes per cubic millimeter, with 86% polymorphonuclear leukocytes.

On Aug. 22, at 9:00 p. m., a septal abscess was incised on each side of the septum, with liberation of blood and pus. On Aug. 23 the patient appeared generally worse, with increasing edema over the bridge of the nose and of the nasal septum. The right eye had become more edematous, with beginning proptosis and chemosis. The left eye was not as prominent as it had been upon admission.

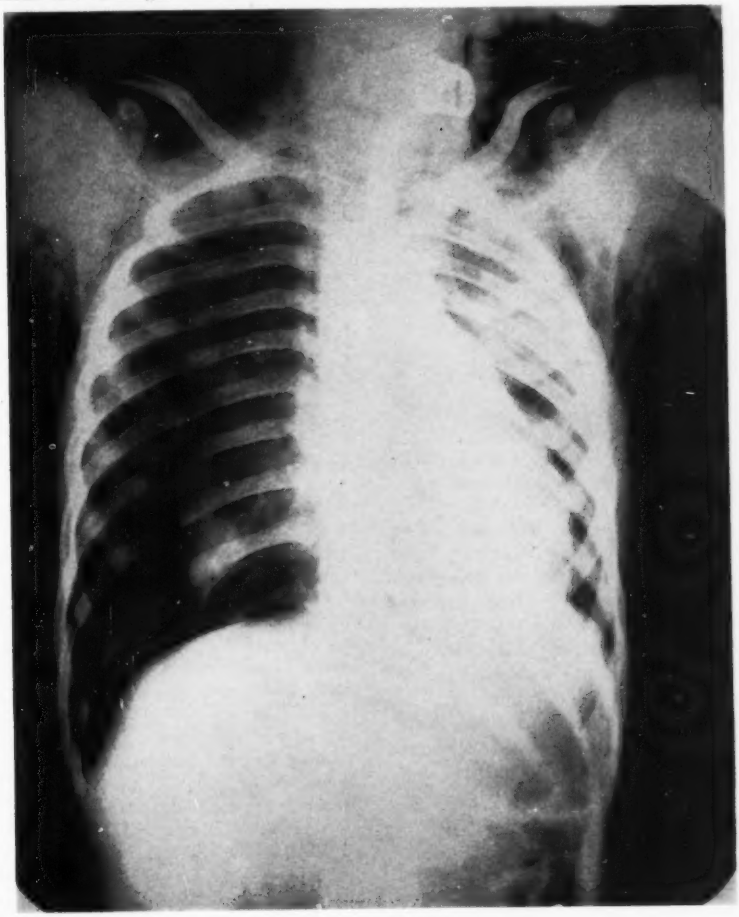
Examination by a neurosurgical consultant showed edema over the bridge of the nose, over the medial part of the forehead, and over both periorbital areas. There was pale chemosis on the right. No movement of the right eye was possible, and there was slight proptosis; the right pupil did not react to light. Both fundi appeared normal. It was the consultant's impression that the patient had a suppurative sinusitits with orbital cellulitis. Examination of nasal exudate by smear showed large numbers of Gram-positive cocci, singly, diploid, and in short chains. A Gram stain of the spinal fluid showed similar organisms. Both materials were submitted for culture.

On Aug. 23, at 10:00 p. m., an ethmoidotomy was performed, but no pus was found in the ethmoid sinuses. The following morning, his neck

was more supple, but his temperature was still 40 C (104 F). At this time he was unresponsive. He was placed on treatment with penicillin, streptomycin, tetracycline, and heparin. Later in the day, his temperature declined, and his urine output increased. The patient had an involuntary stool. The spinal fluid grew out a coagulase-positive hemolytic S. aureus, as did the nasal exudate. The organism was susceptible to all antibiotics tested. At 7:30 that evening a tracheostomy was done. At 12:15 a. m. on Aug. 25 the child became very spastic. Coarse rhonchi and rales developed in the left lung, and he no longer reacted to painful stimuli. By 11:00 p. m. that night the patient seemed much improved, and his tracheostomy was functioning well. The patient had ceased to be spastic and reacted to painful stimuli. On Aug. 26 he became more responsive and answered to his name, as well as reacting to painful stimuli.

On Aug. 27, at 7:30 p. m., the patient suddenly developed a left tension pneumothorax, which was treated by a No. 40 tube placed in the pleural cavity. At 11:00 p. m. that evening he developed clinical and radiological signs of a right pneumothorax (Fig. 20), and 5200 cc. of air was removed. A No. 34 Pezzer catheter was placed in the right pleural cavity. On Aug. 28 the heparin was discontinued. On Aug. 28 at 8:00 p. m. his respiratory state was no different than it had been, and he continued with an elevated rate and depth. Treatment was continued with the previously administered antibiotics, and erythromycin and novobiocin were added. On Aug. 29 he seemed a little improved, but his condition remained critical. His

Fig. 20 (Case 5).—Right pneumothorax following left pneumothorax, which was treated by intercostal tube drainage.



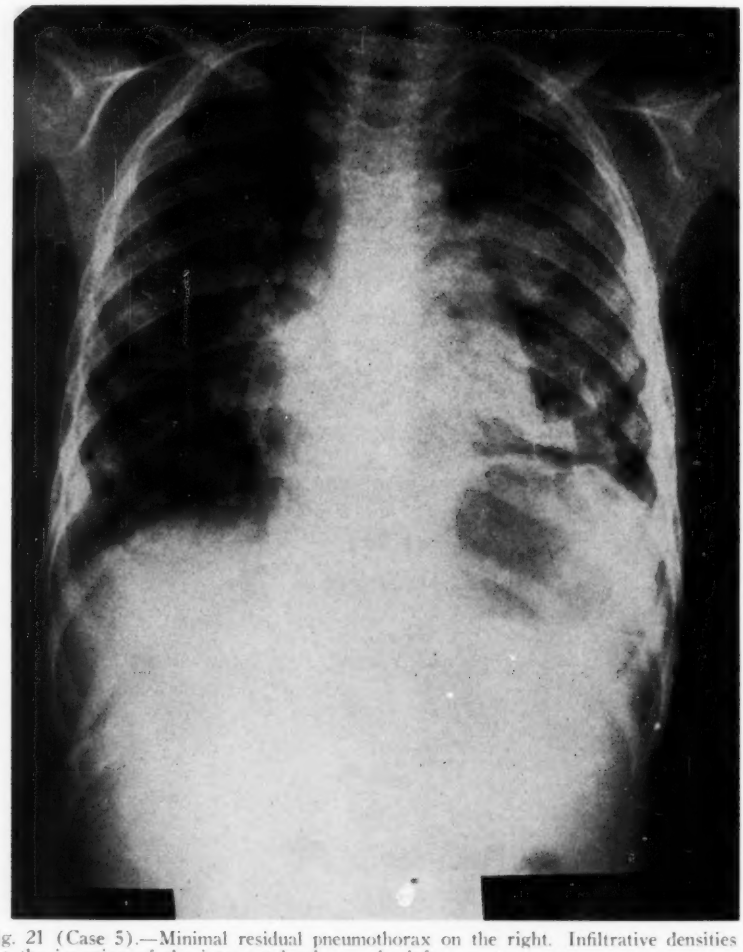


Fig. 21 (Case 5).—Minimal residual pneumothorax on the right. Infiltrative densities seen about the insertion of the intercostal tube on the left.

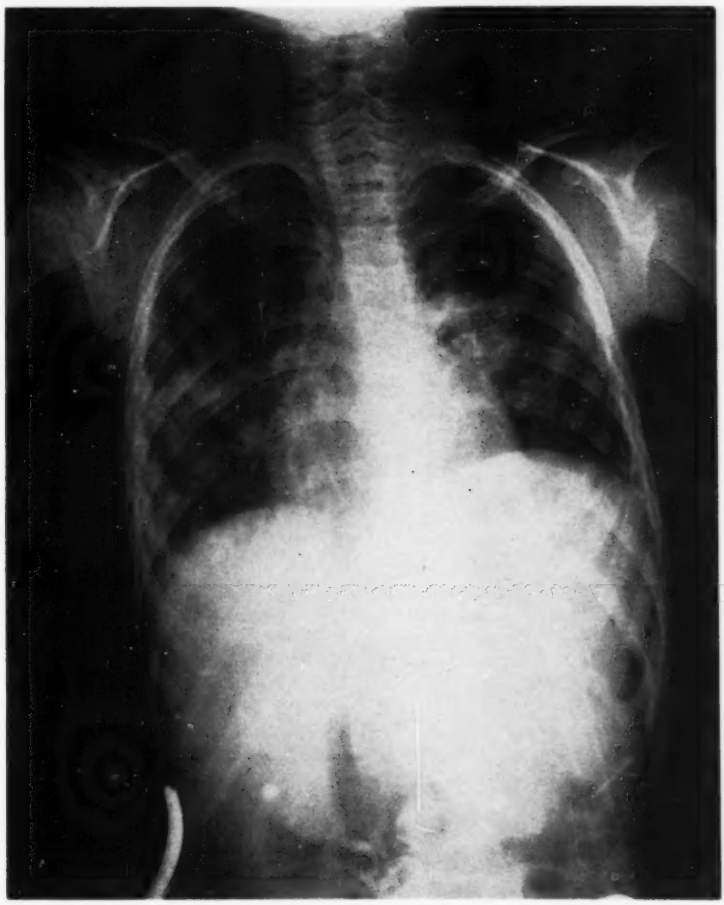
respiratory rate was extremely rapid and shallow, with poor exchange. Both chest tubes were fluctuating well. Repeated spinal tap at this time showed Gram-positive cocci upon smear. From the nasal wound 20 to 30 cc. of pus continued to drain daily. He was given blood transfusion. At 10:00 p. m. that evening the patient had a decrease in rate and depth of respiration, became apneic, and sustained a cardiac arrest. Epinephrine was administered into the myocardium, and artificial respiration was started. The child responded dramatically, and he was placed on positive-pressure oxygen therapy, with some slowing of respiratory rate. At this time he responded to verbal stimuli and moved his extremities. Twelve hours later he was responding to questions and moved all four extremities. His temperature was 38.3 C (100.9 F), pulse 116, respiration 32, and blood pressure 116/50. Treatment was continued with erythromycin, novobiocin, penicillin, streptomycin, and sulfadiazine. On Sept. 2 the left chest tube was removed. At this time he exhibited paralysis of both lateral rectus muscles. On Sept. 3 the patient had a spiking temperature, with elevation to 40 C (104 F), and later that day he developed another left pneumothorax, which was managed by replacing the intercostal closed drainage tube. The roentgenogram (Fig. 21) shows a minimal residual pneumothorax on the right. Infiltrative densities are seen about the insertion of the intercostal tube on the left. On Sept. 5 he again had a spiking temperature, to 39 C (102.2 F), and x-rays showed evidences of bilateral pneumonia. The

roentgenogram taken on Sept. 8 (Fig. 22) shows intercostal closed drainage tubes present bilaterally. There are areas in the right lung field with the appearance of round cavities, which may be abscesses or pneumatoceles; one in the right costophrenic angle had enlarged somewhat since the previous examination. In the left midlung field there is considerable reaction around the site of the chest tube or possibly a pneumatocele. On Sept. 18 the roentgenogram (Fig. 23) shows slight clearing of the density just to the left of the left hilus. The pneumatocele in the right costophrenic angle persists. On Sept. 20 his right chest tube was removed without incident, and on Sept. 23 his left chest tube was clamped, to be removed on Sept. 25. Roentgenographic examination on Sept. 27 (Fig. 24) showed infiltrative densities in both midlung fields, more marked on the left.

His clinical course continuously improved, with complete clearing of the roentgenograms of the chest over a three-month interval. His only residual lesion has been a bilateral paralysis of the lateral rectus muscles.

The pneumonitis in this case was secondary to a hematogenous spread from an orbital cellulitis produced by a nasal-septum abscess. Despite the difference in pathogenesis of the pneumonitis, the tendency to spontaneous pneumothorax and the usual pleural complications is striking. This

Fig. 22 (Case 5).—Bilateral intercostal tubes in place. Infiltrative densities in both midlung fields, more marked on the left. There are areas in the right lung field with the appearance of pneumatoceles.



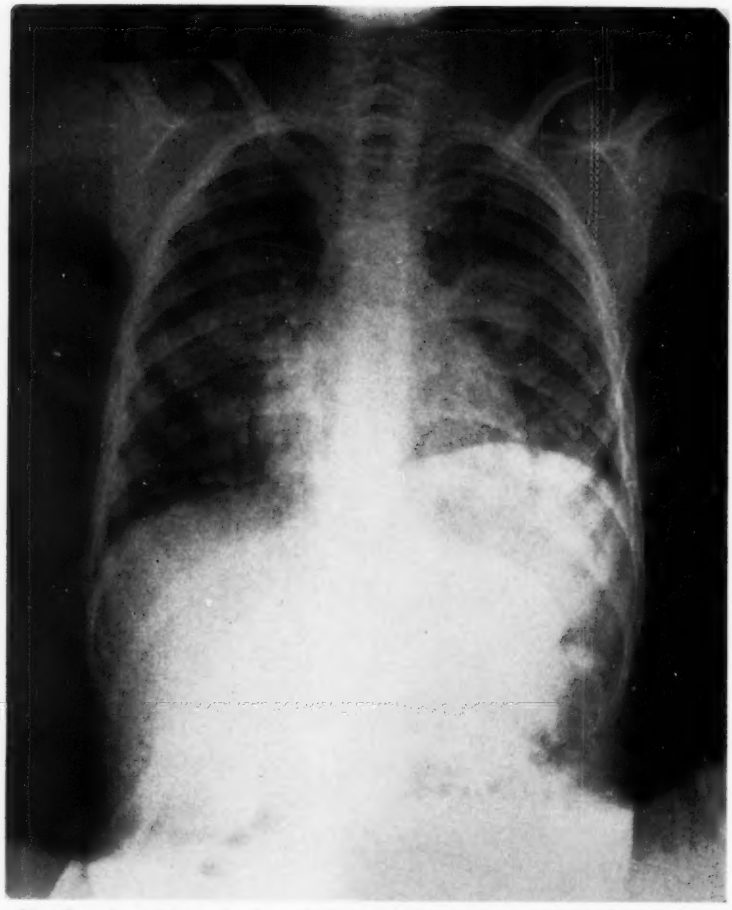


Fig. 23 (Case 5).—Slight clearing of the density just to the left of the left hilus. The pneumatocele in the right costophrenic angle persists.

tendency to recur and occur late in the course of the infection is marked.

CASE 6.—F., a 19-day-old, premature female infant, who weighed 1410 gm. at birth, became more lethargic than before, the condition beginning about 12 hours before she was seen by the surgical service. It had been noted that she was becoming cyanotic during feeding. This condition gradually became worse. X-ray examination of the chest showed a marked left tension pneumothorax (Fig. 25). Thoracentesis was performed, with the removal of about 15 cc. of air under tension. A No. 8 F. rubber catheter was inserted into the third intercostal space, and it continued to blow air. Only about 0.5 cc. of pus was removed, and this positive, was obtained. Repeat films showed that the lung expanded well, but with a small degree of pneumothorax in the opposite side (Fig. 26). She was placed on erythromycin, chloramphenicol, and penicillin.

was cultured and a hemolytic S. aureus, coagulase-

On Jan. 13, 1957, the child exhibited increasing abdominal distention, with episodes of apnea and circumoral cyanosis. However, good breath sounds were heard bilaterally. No bowel sounds were heard in the abdomen, and the child continued to have abdominal distention. On Jan. 14 no more purulent material was being aspirated from the chest. On Jan. 15 breath sounds and bowel sounds were both good, and the abdomen was softly distended. During the day the distention became greatly reduced, and stool was passed after a 10 cc. water enema. At this time, a chest roentgenogram (Fig. 27) showed almost complete expansion,

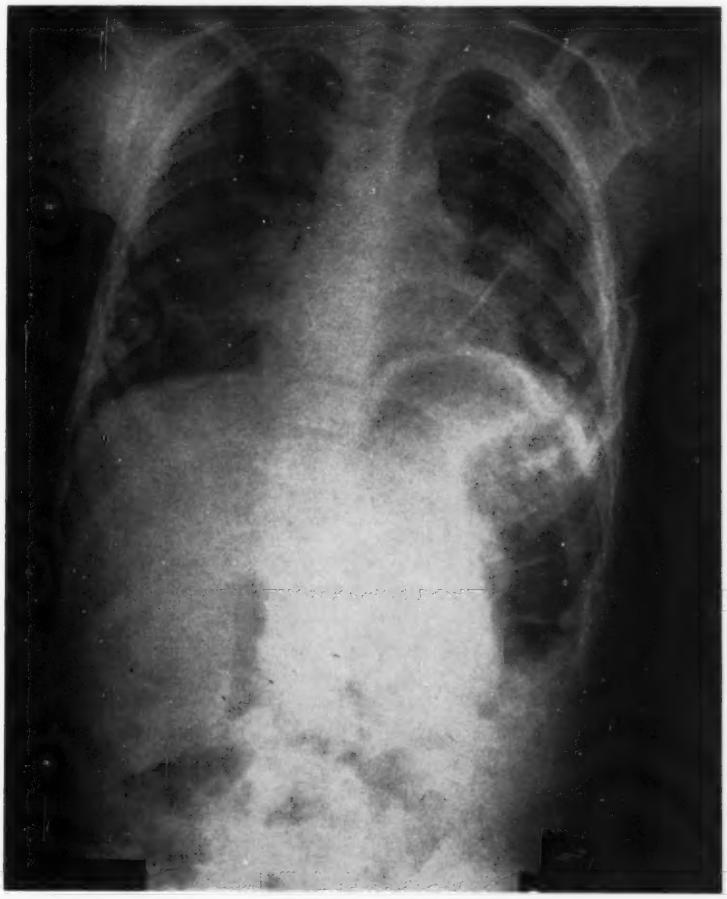
and the chest tube was removed. On Jan. 17 the baby was doing well and weighed 1250 gm. On Jan. 27 at 10:00 p. m. the child had a sudden elevation of temperature to 40 C (104 F). There was no evidence of illness otherwise. The chest film at this time appeared negative (Fig. 28), and there was no growth of organisms on blood culture. The antibiotics were stopped on Jan. 30, and there were no further significant temperature elevations. The child continued to do well and was discharged home on Feb. 23, 1957.

This case represents a favorable response of the parenchymal lesion to antibiotic therapy and a favorable response of the pleural complication to closed intercostal drainage. The complete clearing of the roentgenogram and the favorable clinical course are evidences for the resolution of the pneumonic process.

Comment

In the early stages the presenting symptoms and signs may be somewhat variable. In many instances the overt symptoms of pneumonitis are preceded by those of an upper respiratory infection, from which the expected features of fever, cough, and rapid, grunting respirations gradually proceed. In some patients the onset of pneumonitis is insidious, with symptoms and signs mimicking those of a pneumococcal infection. In others, particularly in very young infants,

Fig. 24 (Case 5).—Infiltrative densities in both midlung fields, more marked on left. Disappearance of pneumatocele on right costophrenic angle.



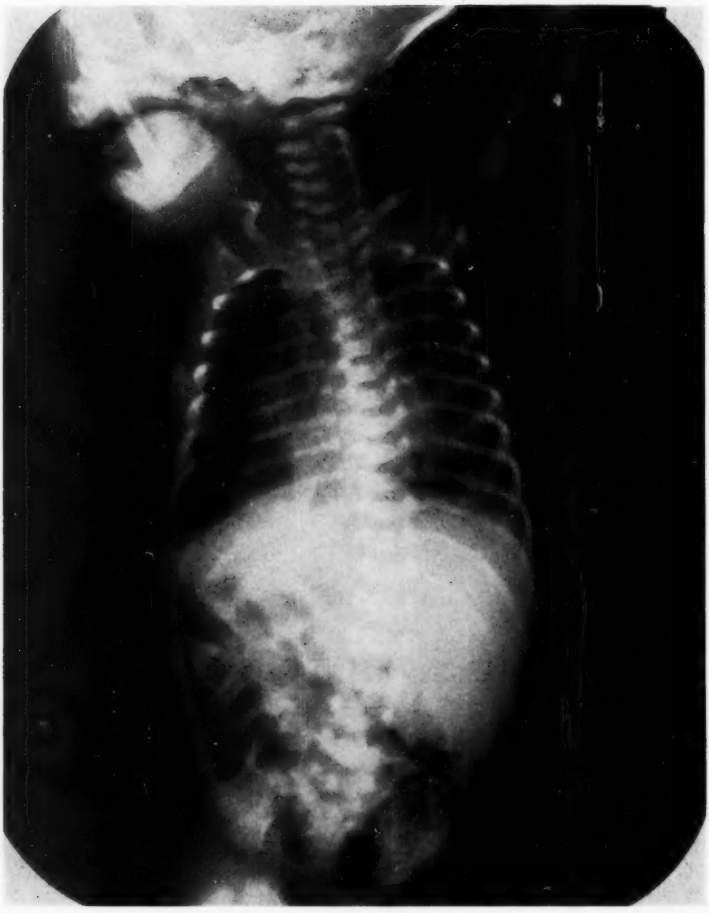


Fig. 25 (Case 6).—Left pneumothorax.

the course is a fulminating one, with the usual clinical picture of pneumonitis overshadowed by toxemia with prostration, cyanosis, extreme dyspnea, and shock, death occurring within a day or two of onset. Gastrointestinal symptoms, especially abdominal distention, are common. In those infants in whom pyopneumothorax occurs, the change in the symptomatology is often rather characteristic. Symptoms of pneumonitis progress for a day or two, when a sudden turn for the worse occurs. The infant shows a marked increase in respiratory difficulty, exhibits cyanosis and prostration, and may appear moribund. These episodes are believed to be associated with a tension pneumothorax. This type of clinical progress should strongly suggest the possibility of a staphylococcal infection. In other patients the course is a relapsing one, with repeated episodes of pneumonitis.

Upon physical examination signs of consolidation are frequently elicited. If pleural effusion or empyema is present, characteristic signs can be obtained over the entire involved hemithorax. A flat percussion note and diminution in breath sounds are characteristic; respiratory lag, tracheal and cardiac shift, and fullness of the intercostal spaces complete the picture. However, breath

sounds in young infants may be heard quite well through an area of effusion, and the detection of areas of consolidation is much more difficult than in the older child or the adult. Fever and respiratory distress are common, and in severely ill infants, prostration, cyanosis, and even shock may be present.

In the roentgenogram infiltrative lesions characterize the early stages of the disease. These vary in distribution from segmental and lobar to focal and diffuse. The multiple small abscesses are usually not recognizable as such. There is often nothing to distinguish the picture from other types of bacterial pneumonia. In the presence of a pleural effusion or empyema the involved hemithorax of the young infant presents a picture of uniform homogeneous opacification. Shift of the mediastinum is often demonstrable. In older patients, pleural involvement may be more localized. Pyopneumothorax is relatively common. Air as well as fluid is seen in the pleural space in about one-third of cases with pleural involvement. In an occasional case a patient may present only abnormal physical signs due to a pneumothorax, associated with a relatively small

Fig. 26 (Case 6).—Left lung expanded with small residual pneumothorax. Small pneumothorax on right.

Fig. 27 (Case 6).—Almost complete expansion both lungs. Slight residual pneumothorax on left.

amount of pus. The extent of the pneumothorax is variable, and it is most easily visualized in films taken in the upright position. It may be so extensive as to suggest a diagnosis of spontaneous pneumothorax, and the air may be under considerable tension. Tension pneumothorax is most apt to be seen in the young infant with profound respiratory embarrassment.

Pulmonary pneumatoceles are most commonly seen following the initial stage. These usually appear as thin-walled, cyst-like cavities situated in the pulmonary parenchyma. Characteristically, they produce no symptoms and persist for weeks or months, gradually diminishing in size. They are rarely seen in other types of pneumonia and are of considerable diagnostic value.

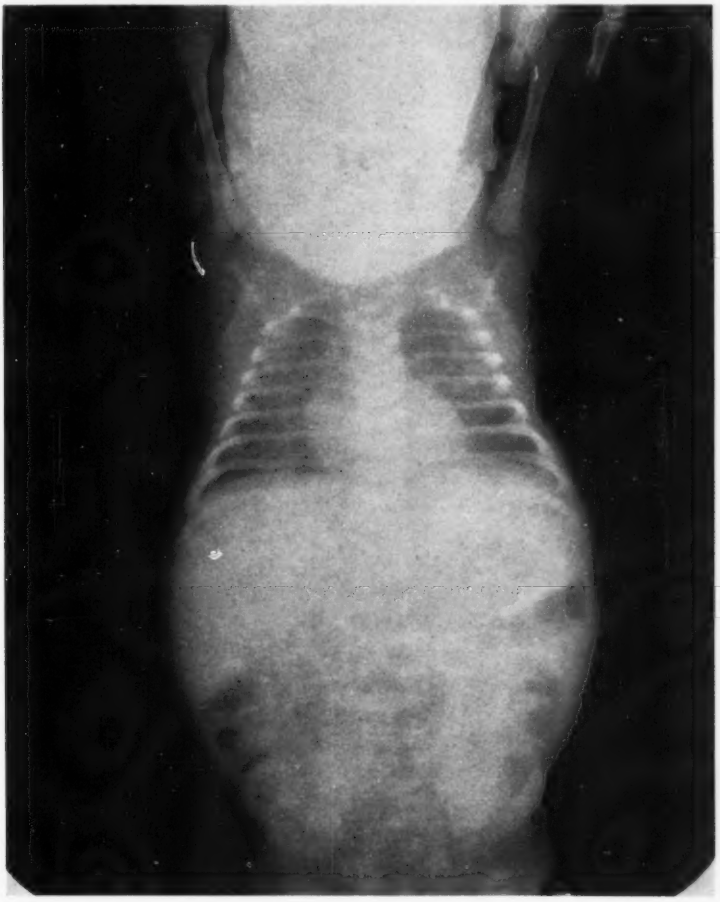
Diagnosis may present some difficulty in the early stages, when the clinical and roentgenographic picture may resemble that of pneumococcal pneumonia. The recovery of staphylococci from the blood or pleural fluid is confirmatory, and a pure culture from the nasopharynx is highly suggestive. A definitive bacteriologic diagnosis is fre-

quently rendered difficult by the early exhibition of antibiotic drugs to such patients. The presence of foci of staphylococci elsewhere in the body may provide a helpful indication of the true etiology. The rapid and gratifying response of the usual case of pneumococcal pneumonia to penicillin therapy is so uniform that the absence of such response should suggest another cause for the pneumonitis. The age incidence curve for staphylococcal empyema is so striking that the occurrence of empyema in a young infant is strong evidence in favor of staphylococcal etiology. Pyopneumothorax is diagnostic; during convalescence the occurrence of pulmonary pneumatoceles is highly suggestive.

Treatment

The primary therapy of staphylococcal pneumonitis is medical, and the therapy is aimed at eradication of the infecting organisms by the systematic administration of antibiotic drugs. Penicillin was formerly a most effective agent, but with the development of strains of staphylococci resistant to this agent, other antibiotics in common use, such as chloramphenicol and the various tetracyclines, have replaced penicillin. In cases in which the organisms are insensitive

Fig. 28 (Case 6).—Complete recovery and negative chest film.



to these drugs, others, such as erythromycin, carbomycin, and novobiocin are useful.

The anticipated complications of staphylococcal pneumonitis which require surgery are empyema, bronchopleural fistula, tension pneumothorax, fibrothorax, and occasional abscess formation. The commest indication for surgical intervention is the development of the pleural complications of the disease. These often develop suddenly and if untreated, may lead to death. There may be a rapidly developing empyema and bronchopleural fistula, which may be sufficiently large to produce a tension pneumothorax. Such events lead to overwhelming infection and respiratory embarrassment. Closed suction drainage is the treatment of choice.[15,16] Usually this leads to reexpansion of the lung, with obliteration of the pleural space and control of the suppurative process. In cases of bronchopleural fistula air may accumulate to produce a tension pneumothorax. Suction drainage here serves to relieve the respiratory distress of pulmonary compression, to evacuate infected material, and to obliterate the pleural space, thus leading to healing.

Pulmonary resection should be reserved for residual lesions which have proved to be sources of recurrent difficulties; the pleural complications of staphylococcal pneumonitis are frequently the result of small pulmonary lesions. Fibrothorax should be avoided by early successful drainage procedures. When fibrothorax does occur, however, decortication is indicated.[17] However, this should not be done unnecessarily early in the course of the disease; many of the changes seen in the roentgenograms disappear over a period of some weeks. Once the pleural complications are dealt with, the prognosis depends on the underlying pulmonary disease. Thoracentesis alone is usually inadequate to control the staphylococcal empyema. When the pus is minimal in amount, however, thoracentesis may be used at first. If repeated aspirations do not produce satisfactory results, early closed drainage of the empyema is indicated.

When the empyema is loculated late in the course of treatment and the lung is encased by thickened membrane and peel, pulmonary decortication may be the preferable procedure. This is also indicated in staphylococcal empyemas with persistent bronchopleural fistula. This measure enables the lung and fistula site to adhere to the chest wall and produce closure of the fistula.

Conclusions

Staphylococcal pneumonitis may produce death from its pleural complications of pneumothorax, pyopneumothorax, and empyema.

The pleural complications of staphylococcal pneumonitis are so common as to be considered an integral part of the disease.

The pleural complications are very frequently bilateral.

Closed intercostal tube drainage in our hands has been satisfactory to manage the pleural complications.

The prognosis depends not only upon the proper management of the pleural complications but also upon the course of the parenchymal lesions.

With increasing development of resistant staphylococci, especially in hospital environments, awareness of this lesion must be heightened, especially in the very young and very old and in those debilitated by other diseases and conditions.

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The Clinical Use of an Elastic Dacron Prosthesis

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The importance of the quality of elasticity in a plastic arterial prosthesis is being generally recognized. While in some anatomical locations, and with rather strict limitations on the length of the segments to be replaced, rigid prostheses may perform well, from the viewpoint of wide-range usefulness the ability to elongate and flex without deformity is an essential characteristic of arterial substitutes. As abundantly proved by both clinical and experimental [1] evidence, without this quality a plastic arterial implant will buckle whenever the anatomical circumstances require bending, and the result of buckling is almost invariably thrombosis. We have formerly described [2] a plastic tube partly composed of specially processed ("Helanca") nylon yarn, which possessed the quality of stretchability. Unfortunately, in experimental studies, while yielding excellent patency rates, the stretch-nylon prosthesis disclosed unsatisfactory durability. More recently a prosthesis of similar construction, but made of Dacron * yarn, has been developed and has given very satisfactory results with respect to the permanence of its tensile strength after implantation. This report is concerned with a summary of the experimental background and a description of the clinical use of this prosthesis.

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From the Department of Surgery, Henry Ford Hospital.

Read at the 15th Annual Assembly of the Central Surgical Association Columbus, Ohio, Feb. 21, 1958.

The experimental work reported was in part supported by a grant from the Michigan Heart Association.

* Dacron is the registered trade name of E. I. du Pont de Nemours & Company for their polyester fiber.

Experimental Studies

Characteristics of the Prosthesis

The prosthesis is woven with a taffeta weave and is seamless. As disposed in the tubular fabric, the longitudinal threads forming the warp are made up of fibers that have been specially processed (Fig. 1); the transverse threads, or woof, or filling, consist of untreated Dacron fibers. The special process

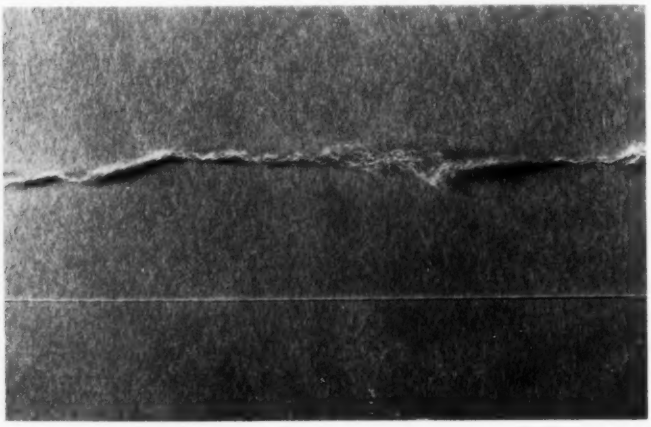

Fig. 1.—Dacron yarn unstretched (above) and under tension (below). The ability to elongate comes from the uncurling of the fibers when put on stretch.

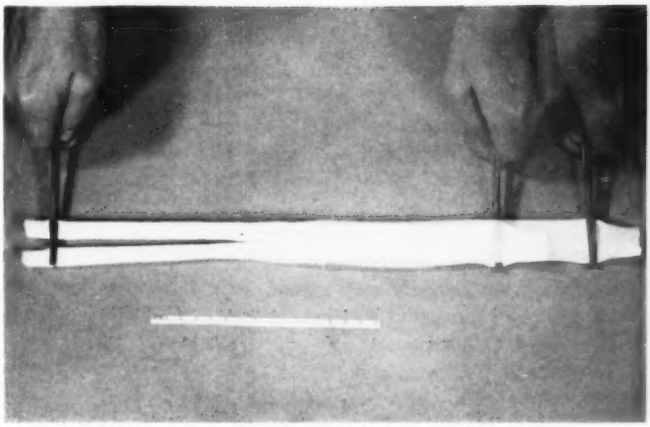

Fig. 2.—Double exposure of a bifurcation prosthesis, showing the range of stretch of the fabric.

to which the fibers of the warp yarn have been subjected is the same as that used for the manufacture of Helanca nylon fiber. In this process the fibers are twisted into tight spirals and then are heat-set. Fibers of opposite directions of twist are combined into the yarn in about equal amounts in order to assure balance. The fibers are stretchable, since on pull the spirals uncurl; when the pulling force is released, the fibers shorten, owing to a tendency to resume their heat-set spiral shape. When yarn composed of such fibers is woven into fabric, this quality of elasticity is largely retained. It is necessary, however, to boil the fabric in liquid soap to restore complete resiliency.

TABLE 1.—*Textile Characteristics of Elastic Dacron Prosthesis*

Diameter, Mm.	Ends/Cm. (Warp)	Elastic Dacron	Picks/Cm. (Woof)	Filling (Woof)
10	80 to 100	70/2	47	220

The yarn in the warp: 70-denier, 2-ply, 70-14 Bright Type 51 dacron.
The yarn in the woof: 220-denier, 220-50 Bright Type 51 dacron.

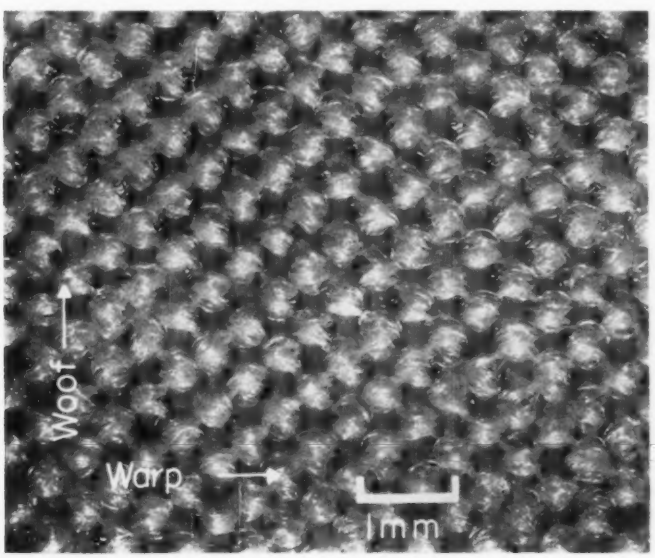

Fig. 3.—Simple taffeta weave of the Dacron fabric. It is the fluffy-appearing strands forming the warp (horizontal in this photograph) that have the quality of elasticity. The meshes vary in size from 0.1 to 0.2 mm. in diameter.

(The contact with soap leaves no deleterious effects, provided the fabric is thoroughly rinsed.) The finished tube can elongate 15%-20% without deformity (Fig. 2).

The textile characteristics of the prostheses used experimentally are given in Table 1. The porosity of the fabric can be judged from the photomicrograph reproduced in Figure 3. The mesh size and the weight of the yarn were arrived at after many experimental trials and appeared to fulfill optimally the basic criterion of minimum bulk with maximum strength. The porosity is such that preclotting is necessary. The technique of this maneuver, as well as a description of some handling and technical details, will be given presently in course of the clinical discussion.

The experimental prostheses were sterilized by boiling; chemical sterilization is also effective (see below). Because of the type of weave used, it is necessary to heat-seal the cut ends of the tubes; this is best done with an electric cautery.

Experimental Surgical Technique

The experimental preparation was that first described by McCune[3] and slightly modified by us. The details of the operative technique were given in full in earlier publications.[1,2] Briefly, the procedure consists in implanting a bypass between the upper thoracic and the lower abdominal canine aorta, the proximal anastomosis being an end-to-end one, thus assuring a complete shunting of the aortic blood into the prosthesis. The method permits the insertion of implants 18-26 cm. in length and 7-10 mm. in diameter, depending on the size of the animal. We believe that this preparation affords a much more realistic test of a prosthesis than the customary short-segment replacements, in many of which the bridging effect of the healing process of the stumps of the host aorta is difficult or impossible to distinguish from the histologic changes peculiar to arteriogenesis. Twenty-one such preparations were made.

Frequent, periodic observations were made regarding the general condition of the host and the quality of the pulses distal to the prosthesis. The state of the implants was followed with interval aortography by percutaneous transthoracic left ventricular injection of approximately 8-10 ml. of 70% sodium acetrizoate (Urokon Sodium). The intervals at which the animals were autopsied were 4 and 30 days; 1, 3, 4, 6, and 9 months. Agonal aortograms at the time of killing were obtained through a left thoracotomy by direct injection into the thoracic arota. All prostheses were removed and their gross characteristics noted and recorded. Appropriate photographs were taken and representative microscopic sections made. The tensile-strength characteristics of the prostheses were determined with the Instron instrument.* With normal fresh dog aorta and samples of new, unused prostheses serving as standards, representative specimens recovered at two, four, six, and

* The Instron instrument incorporates a highly sensitive electronic weighing system employing bonded-wire strain gauge for detecting and recording the load applied to the sample under test. Dr. V. Zackay and his associates of the Research Laboratories of the Ford Motor Company, Detroit, gave us assistance in obtaining these measurements.

TABLE 2.—*Findings of Experimental Study: Autopsied Animals*

Dog No.	Length of Follow-Up, Mo.	Length of Prosthesis, Cm.	Diameter of Prosthesis, Mm.	Fate of Host	Aorto-gram	Reaction Around Graft *	Luminal Surface †	Results	Comments
LF 138	4 days	21	10	Died	None	—	—	Satis.	Wound disruption
LF 128	1	20	10	Died	Patent	+	Patchy	Good	Pneumonia
LF 145	1	21	10	Died	Patent	++	Patchy	Satis.	Distemper
LF 143	3	18	10	Killed	Patent	+	Patchy	Good	Distemper
RM 92	4	20	10	Killed	Patent	+	I & S	Good	
LF 126	4	22	10	Died	Patent	++	I & S	Good	Pneumonia
RM 87	6	23	10	Killed	Patent	+	Incomp.	Satis.	Pseudointima almost complete
RM 94	6	20	10	Died	Patent	+	I & S	Good	Distemper
RM 95	9	20	10	Killed	Patent	+	I & S	Good	Extraluminal fibrosis at diaphragm
RM 97	9	23	10	Killed	Patent	+	I & S	Good	

* Adventitial reaction: +, very thin layer; ++, less than 1 mm. thick.
† I & S: Intact and smooth.

TABLE 3.—*Findings of Experimental Study: Living Animals*

Dog No.	Length of Follow-Up, Mo.	Length of Graft, Cm.	Diameter of Graft, Mm.	Fate of Host *	Aortogram	Distal Pulses	Nutritional Status
LF 148	5	20	10	L & W	None	Good	Normal
LF 147	5	22	10	L & W	None	Good	Normal
LF 144	5	21	10	L & W	None	Good	Normal
LF 142	6	19	10	L & W	None	Good	Normal
LF 140	6	26	10	L & W	Normal	Good	Thin
LF 139	6	20	10	L & W	Normal	Good	Normal
LF 136	6	20	10	L & W	None	Good	Normal
LF 125	7	20	10	L & W	Normal	Good	Normal
LF 122	7	20	10	L & W	Normal	Good	Normal
RM 96	10	19	10	L & W	Normal	Good	Normal
RM 93	11	20	10	L & W	Normal	Good	Normal

* L & W: Living and well.

nine months were tested. Identical dumbbell-shaped samples were cut with a die in the longitudinal axis of the prosthesis, with a central, or test, area 0.5 in. in width. The rate of pull was constant, at 1 in. per minute. It was elected to test the full thickness of the wall of the recovered graft, for it is the combination of the prosthesis and its fibrous tissue sheath that replaces the artery and withstands the stress.

Results

The findings with respect to the function and fate of the prosthetic implants in the 10 animals that came to autopsy are listed

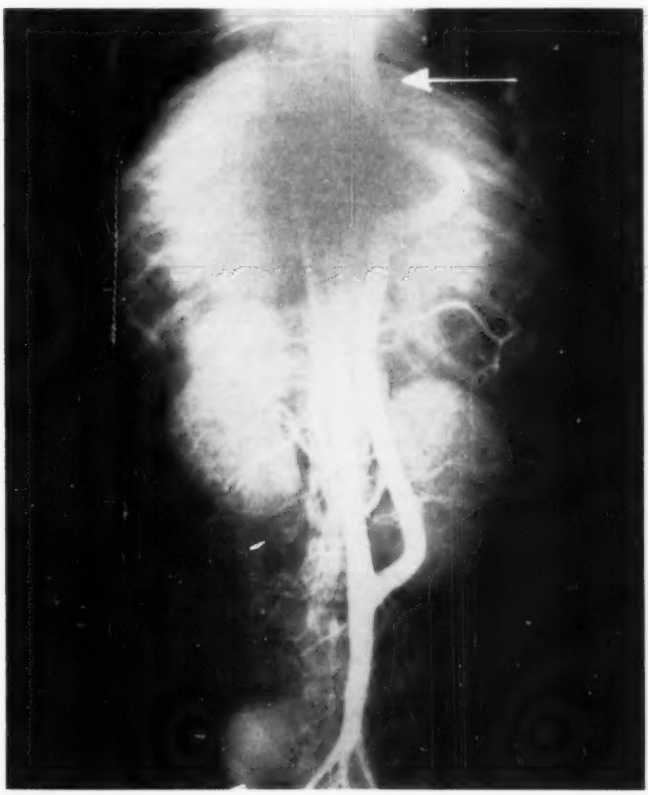

Fig. 4.—Aortogram of canine implant taken six months after insertion. The prosthesis follows a tortuous course.

Fig. 5.—Gross appearance of a canine implant six months after insertion. The fabric is completely covered by a smooth, flawless pseudointima about 0.5 mm. in thickness. The connective tissue shell and ingrowth are firmly adherent to the fabric, and thin but sturdy. The mean total thickness of the new artery is 1.5-2.0 mm.

in Table 2. Among the 21 experimental animals, 5 were killed on schedule, and 5 died of intercurrent causes. The causes of death in the latter group were pneumonia (in two), distemper (in two), and wound disruption. No causal relation existed between the behavior of the implants and these deaths. The state of nutrition and health of the animals now under observation (Table 3) is very satisfactory, and so was that of the animals that were killed according to the experimental plan. This observation is noteworthy, since even partial occlusion of the aortic bypass leads to serious cachexia. (It will be recalled that in the experimental preparation blood reaches the abdominal viscera in a retrograde manner; any interference with this blood flow results in physiological disturbances at the visceral level.) The aortographic appearances of the prostheses one to six months postoperatively in six animals still living have been normal. This was true also of those prostheses that, by design, had a tortuous course (Fig. 4).

Arteriogenesis around the implants was, in most respects, excellent. *Grossly* (Figs. 5 and 6), the connective tissue reaction was adequate but not excessive. The pseudointima appeared smooth and intact in most instances, but in early specimens occasionally patchy ulcerations were seen. The impression was that the formation of the new inner lining was not quite as rapid as we have observed in nylon prostheses. This imperfection was, however, a relative one, evident only in comparison with the nylon implants, which in our experience yield a particularly satisfactory pseudointima, and never severe enough to result in thrombosis. *Microscopically* (Fig. 7), the most striking characteristic of the histologic process around the implants was the nearly complete lack of cellular exudation. In this respect we found the lack of reactivity of these Dacron prostheses comparable to that of Teflon tubes. The connective tissue proliferation was orderly and adequate.

The behavior of the tensile strength of the recovered implants was excellent (Figs. 8 and 9). Starting out with an average tensile strength of 56 lb. per 0.5 in., this factor remained essentially unchanged during the period of observation of nine months. The slight variations noted were undoubtedly due to intrinsic differences among the various fabrics used for implantation and testing.

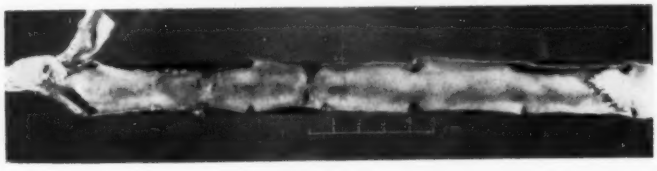

Fig. 6.—Implant nine months after insertion. The appearance is essentially the same as at six months (Fig. 5), but there are two small flecks of thrombus near the midportion where the pseudointima has not been perfectly formed. These flaws did not compromise function, and they would probably have been healed over by organization of the small thrombi.

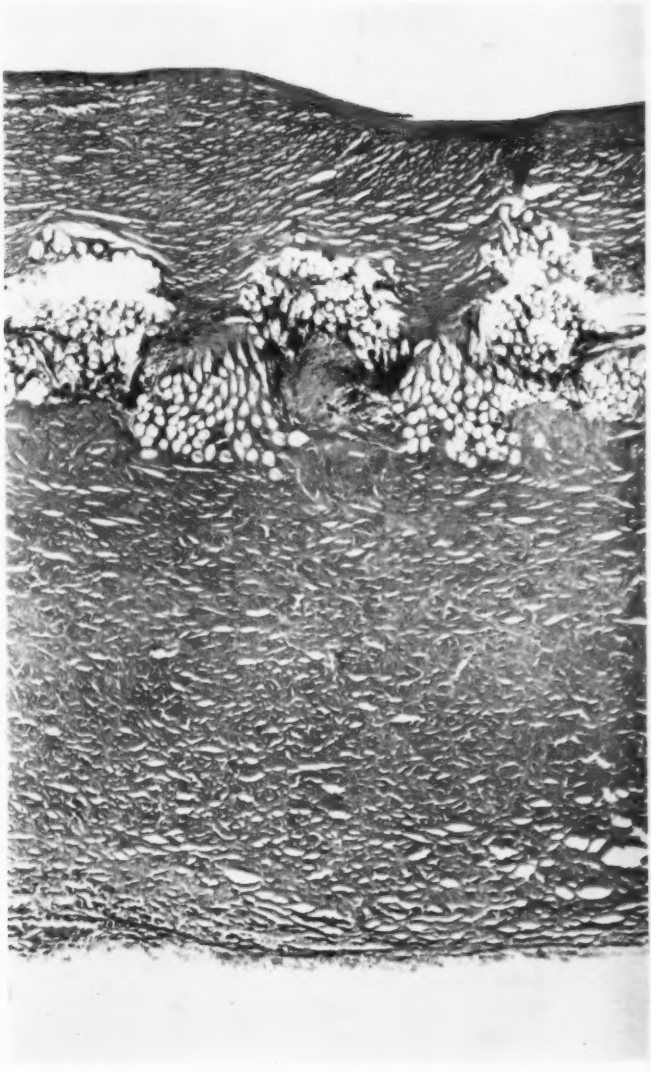

Fig. 7.—Microscopic section of the midportion of implant shown in Figure 6. This is as satisfactory a process of arteriogenesis as we have seen. Cellular exudative reaction is almost completely absent. The growth of connective tissue appears to serve only one purpose: the integration of the plastic fibers into a firm structure. Hematoxylin-eosin stain; reduced to two-thirds of mag. ×70.

Summary of Experimental Observations

The tubular seamless prosthesis woven with elastic (Helanca) Dacron yarn displayed most of the advantageous qualities of the prosthesis made of elastic nylon, and, in addition, it appeared to have marked superiority in its durability after implantation; this last property may be looked upon as the result of the marked nonreactivity of the Dacron yarn.

Clinical Experiences

Properties of the Elastic Dacron Prosthesis

The external appearance of the prosthetic tube of stretch Dacron as used by us is very similar to that made of stretch nylon. It is white (or, rather, colorless), soft, pliable, smooth, light, and moderately porous. On handling it, one is impressed by the lack of bulkiness that is peculiar to knitted or

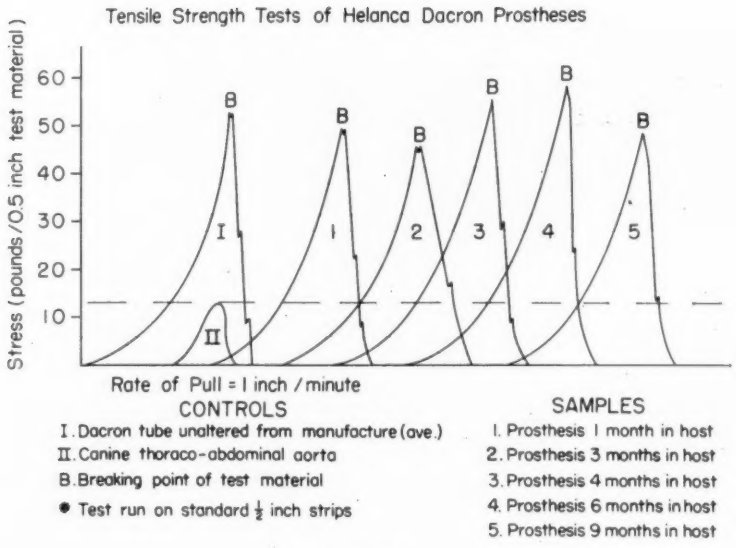

Figure 8

crimped tubes and the absence of stiffness that is characteristic of Teflon textiles. Its most conspicuous defect is its tendency toward "slippage," that is, the ease with which, on manipulation, the strands of yarn in the fabric slide and create faults in the weave, a quality to be discussed below. The prosthesis does not require any special precautions for its storage. It can be sterilized chemically or by boiling and autoclaving. As a sterilizing agent, benzalkonium (Zephiran) chloride in 1:1000 solution for 18 hours of

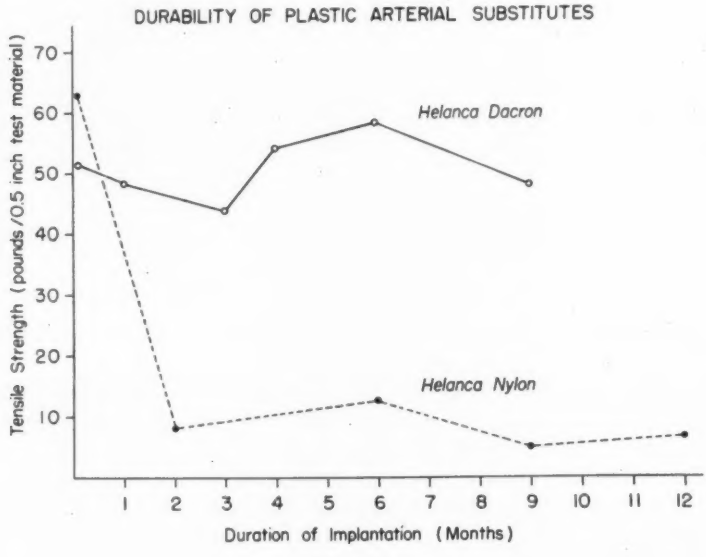

Figure 9

contact has been effective. It should be noted that repeated autoclaving reduces elasticity.

Technical Details in Use of Elastic Dacron Prosthesis

Without some appropriate pretreatment, a fabric of the porosity of the Dacron prosthesis being discussed will leak blood rather vigorously. We have found that by rinsing the inner and outer surfaces of the prosthesis with 15 to 20 ml. of blood obtained from an unheparinized segment of the exposed arterial tree, and by allowing the prosthesis to soak in this blood for three to four minutes, one can bring about just enough clotting to seal off the meshes of the fabric. A moderate amount of oozing may still occur after the prosthesis has been inserted and blood allowed to flow through it, but this can be readily controlled by short periods (20-30 seconds) of occlusion of the inflow while the blood is allowed to remain in the prosthesis. It is of the utmost importance to use great care in the process of clot sealing of the plastic implant. After the in vitro clotting, the prosthesis must be checked for the presence of visible or palpable thrombi; and if any are found, they must be removed by gentle milking or, if necessary, by rinsing with a heparin-saline solution (0.5 mg. of heparin per 1.0 ml. of saline). The same precaution must be observed during the performance of the insertion of the implant. Obviously, stagnant blood is never allowed to remain in the prosthesis once the clot sealing has been accomplished. If, owing to some technical mishap, it becomes necessary to stop the flow of blood through a prosthesis already in place, before the distal clamp is applied the blood is milked out of the implant and the implant is filled with heparin-saline solution until the flow may be reestablished. Leaving a layer of thrombus in the lumen of the prosthesis that is thicker than about 0.1-0.2 mm., or allowing the presence of lumps of clot, may have disastrous consequences. Not only may it delay or prevent the orderly formation of the pseudointima, thus resulting in early occlusion, but it may lead to a rapid, almost immediate, progression of the clotting process to a point where the prosthesis cannot function at all.

The free cut end of a woven fabric tends to unravel, particularly if the component yarn contains smooth-surfaced fibers, as is the case with the elastic Dacron prosthesis. This tendency can be easily corrected, however, by melting and fusing the ends of the cut fibers through the application of heat. We have found it convenient to heat-seal the prosthesis *before* beginning the implantation. The length of the implant is judged by placing a heavy black thread in the exact position the prosthesis is to occupy and by using this measure as the base for the simple calculation. To obtain the desired dimension, 10% to 15% of the length of the thread, is subtracted, depending on the somewhat variable elasticity of the plastic tube. In case of doubt, care is exercised to make the implant slightly longer rather than shorter than is ideal. The ends of the prosthesis of the desired length are cut with scissors at any angle needed for the proposed anastomosis. The cut ends are lightly touched with a flat-tipped electric cautery which has been heated just short of being red. The ideal heat-seal is a narrow (about 1.0 mm.), even, and smooth band of fused plastic which lies exactly in line with the scissors cut. A light touch and attention to technique are necessary for the proficient use of any plastic prosthesis, and they are of special import when dealing with light woven fabrics. The manual handling and the suturing of the elastic Dacron prosthesis demand great gentleness. The prosthesis must not be picked up with instruments having a rough surface, and clamps applied to it must be rubber-shod. If, nevertheless, separation of some of threads occurs, the flaw can usually be corrected by gentle rubbing between fingers. In placing sutures, only the slightest strain is allowed on the fabric.

The optimal size of the prosthesis to be used in a given case is a matter of some doubt. Theoretical arguments can be advanced in favor of the use of implants significantly larger in diameter than the host

TABLE 4.—*Dimensions of Implanted Prostheses*

Prostheses *	No. Cases	Length † (Range in Cm.)	Diameter (Range in Mm.)
Aortic rpl.	1	10	35
Aortoiliac rpl.	11	6 to 11+4 to 8+4 to 7	25 to 30+12+12
Aortofem. bp., unilat.	4	20 to 28	12
Aortofem. bp. bilat.	8	4 to 10+17 to 19 ½+17 to 19 ½	14 to 25+9 to 14+9 to 14
Femoral rpl.	1	4	12
Femoropopl. bp.	17	31 ½ to 37	10 to 12
Popl. bp.	1	27	10

* Rpl., replacement; fem., femoral; popl., popliteal; bp., bypass; unilat., unilateral; bilat., bilateral.
† The mean length of all aortoiliac prostheses was 9+14+13 cm.; the mean length of femoral prostheses was 46.0 cm.

artery, and also in favor of reducing the size of the prosthesis by some small factor. As an empirical proposition, the use of prostheses of approximately the same size as the host artery has appeared to us to be entirely satisfactory. In the femoral and popliteal areas an upward correction of about 2.0 mm. in the inside diameter is made in order to allow for the thickness of the luminal component of the connective tissue conduit to be built by the host.

The technical details enumerated are valid for the straight tubular, as well as for the bifurcated, prostheses. Because of problems inherent in weaving techniques, the undersurface of bifurcations (the so-called "crotch") is not truly seamless. Although we have found that the seal of the weave at the crotch has been consistently strong, it is advisable to inspect this part of the bifurcation prostheses with particular attention before use.

Clinical Material

During the period covered by this report † (June, 1957, to February, 1958), in dealing with arterial lesions requiring correction by angioplastic procedures, we limited ourselves almost entirely to plastic implants (Tables 4 and 5) and to thromboendarteriectomy. Homografts were used only in the rare cases requiring anastomoses to visceral arterial divisions. We have reserved thromboendarteriectomy for instances in which the occlusive process did not extend beyond the bifurcation of the common iliac artery or to those cases of femoral lesions in which the disease process was sharply limited to a segment no longer than 5.0 cm. It can be seen, therefore, that a factor of selectivity was operative and that it was a factor prejudicial to the procedures utilizing plastic prostheses. In general, it was the more advanced and more diffuse lesions that were treated with the last-named methods. This fact must be kept in mind when the results of the operations with plastic prostheses are evaluated.

In the *aortoiliac* area three types of procedure involving the use of plastic prostheses were employed. Direct replacement of the aortoiliac segment was resorted to in aneurysmal disease or in cases in which the occlusive process extended for some distance into the aorta. In instances of

† From a comparison of the dates of commencement of the experimental and clinical work, it will be evident that the clinical application of the prosthesis was not begun until the results of the tensile-strength studies of the two-month animal implants were available. The prosthesis was not used in the aorta until the six-month implants had been tested.

TABLE 5.—*Results of Grafting Procedures with Elastic Dacron Prostheses*

	Immediate				Early			
	Open		Closed		Open		Closed	
Aortoiliac	22	92%	2	8%	22	92%	2	8%
Femoropopliteal	15	79%	4	21%	12	63%	7	37%
Total	37	86%	6	14%	34	80%	9	20%

aortic aneurysm, the entire disease segment was resected and replaced; in occlusive lesions of the aorta, on the other hand, the iliac arteries were not, as a rule, dissected out and replaced. In all operations of direct replacement the proximal anastomoses (prosthesis to aorta) was end-to-end, while the distal anastomoses were end-to-side,

Fig. 10.—*A*, over-all view of the operative field in a bilateral aortofemoral bypass; *B*, close-up view of the intra-abdominal portion of the prosthesis.

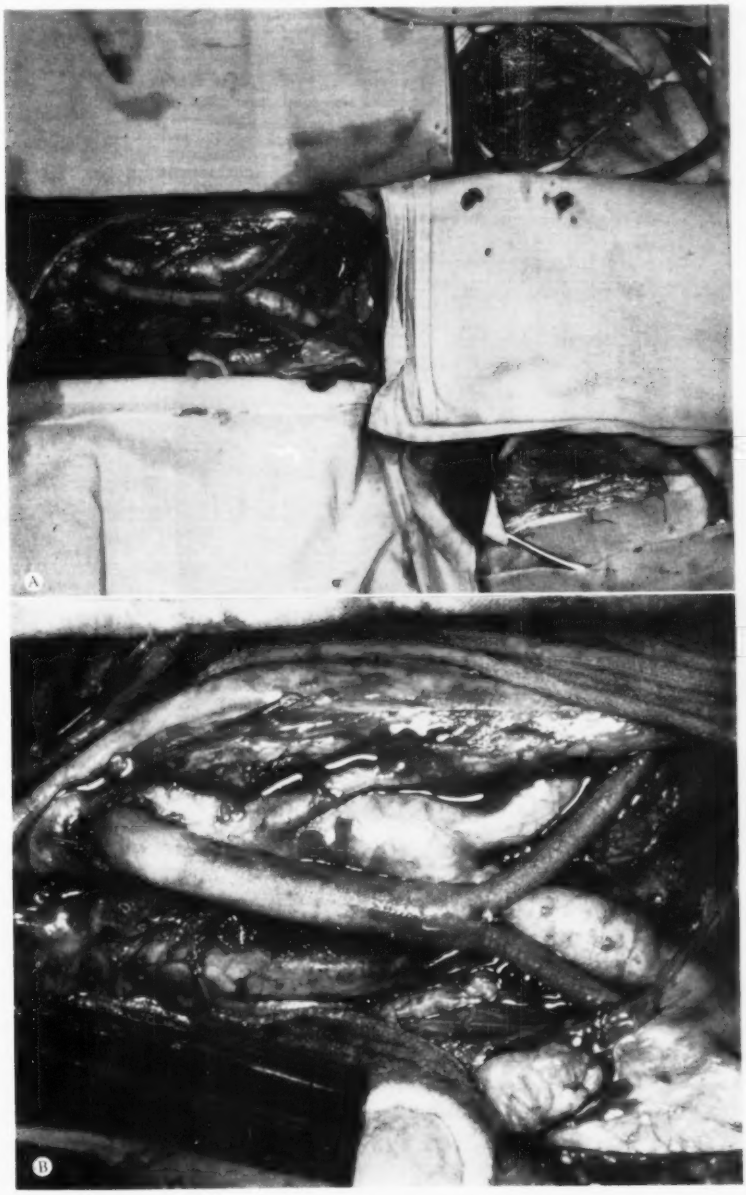

Fig. 11.—Angiographic appearance of the bilateral aortofemoral bypass shown in Figure 10*A* and *B*, six weeks postoperatively.

either at the iliac or at the common femoral level, according to need. In cases of unilateral iliac occlusive disease, when the occlusive process extended beyond the iliac bifurcation, and thus endarteriectomy was deemed unsuitable, aortofemoral bypasses were used, with the proximal anastomosis at the distal aortic level (distal to the origin of the inferior mesenteric artery), and the distal anastomosis at the common femoral level, and with both anastomoses of the end-to-side variety. In extensive bilateral iliac occlusive disease without significant involvement of the aorta, the bilateral aortofemoral bypass was the operation of choice (Figs. 10 and 11). The prosthesis for this procedure was a plastic bifurcation of a size slightly smaller than the respective host vessels; the levels and types of anastomosis were the same as in placement of the unilateral aortofemoral bypass. In the *femoropopliteal* area direct replacement was employed for aneurysmal resection. In occlusive disease the prostheses used were almost exclusively bypasses, virtually all of which extended from the common femoral to the distal popliteal artery, both anastomoses being end-to-side (Fig. 12).

The frequent use of bilateral aortofemoral and of the long femoropopliteal

Fig. 12.—Angiographic appearance of a femoropopliteal bypass with a 57 cm. prosthesis six weeks postoperatively. (The operation was performed after the failure of a homograft that had been in place for three and one-half years. Note markers at the previous distal anastomosis.)

bypasses is another circumstance that emphasizes the severity of the test to which the prosthesis was put in this clinical series. Both these operations are rather complex, and they demand a tortuous placement of the implant; moreover, in the femoropopliteal bypasses the length of the prosthesis is great (without exception in excess of 31.0 cm.), a circumstance that—other factors being equal—is inimical to patency in an arterial replacement.

The types of operative procedures involving the use of elastic Dacron prostheses, the length of the prostheses, and the immediate and early results are listed in Tables 4 and 5. The postoperative periods of observation in these cases ranged from one to nine months. Patency of the graft was always verified by angiography. The results tabulated are cumulative. "Immediate results" denotes the state of the implant at the time of discharge from the hospital; "early results" refers to the condition of the implant at the time of the last angiographic examination up to nine months postoperatively. Clinical examinations were made monthly.

Comment

The Prosthetic Qualities of Elastic Dacron Tubes.

It is our belief that a plastic prosthesis suitable for wide-range clinical use that will yield the best results must combine the following qualities: It must be seamless, smooth-walled, easy to handle, durable, and relatively nonreactive; its porosity and bulk must meet certain critical requirements, and, finally, it must possess the ability to elongate and recoil. (Further important, but not truly essential, requirements for such a prosthesis would be low cost, easy storage, and simplicity of sterilization.)

The reasons for the significance of these attributes are cogent. The presence of a seam and of ridges on the luminal surface of the prosthesis is undesirable, since surface irregularities would increase friction and, therefore, resistance to flow; moreover, and perhaps more important, they would promote excessive clotting along the areas of contact with the blood, a circumstance that, under many conditions, may mean the difference between patency and thrombotic occlusion. The need for ease of handling (as well as for the less essential factors of low cost and simplicity of storage and sterilization) is self-evident. Durability is also an obvious requirement. It is less obvious that durability is largely dependent on lack of tissue reactivity. Regardless of the magnitude of tensile strength that the original fabric possesses, if after implantation the fabric provokes active cellular reaction in the host tissues, it will be attacked by the exudative process and, in the end, will be partly or completely destroyed. The optimal degree of porosity in the fabric is the sum of two requirements: The mesh size must be large enough to allow easy ingress for the ingrowth of connective tissue, but it must also be small enough not to interfere with hemostasis. The restrictions on the bulk (or wall thick-

ness) of the prosthesis are less easy to justify. Undoubtedly, thick-walled, heavy prostheses have served well in many situations during short-term observations. However, a plastic prosthesis is a foreign body, and sound surgical principles would suggest that its mass should be kept to a minimum as long as this restriction does not result in a disadvantage, such as lessening initial tensile strength or durability. While conclusive evidence condemning thick-walled prostheses cannot at this time be cited, it is an easily confirmed observation that the connective tissue reaction around bulky prostheses is excessive, and this is undesirable. The importance of the quality of elasticity has already been discussed. It may be mentioned, however, that the accomplishment of elasticity through specially treated fibers has distinct advantages over methods involving the treatment of the finished tube, namely, crimping, which increases bulk and luminal friction.

While far from ideal, the elastic Dacron prosthesis comes reasonably close to meeting the requirements just enumerated. In construction it is light, seamless, and smooth-walled, providing a porosity that is satisfactory both from the point of view of arteriogenesis and from that of hemostasis. Its tissue reactivity is of the order of that of Teflon, and during the period of experimental observation its tensile strength has remained remarkably stable. It also meets the other prerequisites mentioned that have less fundamental importance but are significant in a practical way.

Some imperfections of the elastic Dacron prosthesis should, however, be pointed out. There is some experimental and clinical evidence that the new-formed lining of the prosthesis is slow to develop, apparently slower than that seen in nylon implants. Since the formation of this pseudointima is greatly influenced by the technique of preclotting, which is largely a matter of personal skill, the evidence in this regard is not entirely clear-cut or convincing. Moreover, in older canine specimens the new intima was always found to be satisfactory. Our attention was directed to the potential importance of this delay in the building of the new prosthetic lining by two instances of thrombotic occlusion, early in our experience, that took place within a few hours after angiography, performed two weeks postoperatively. Angiographic visualization of the prosthesis is now delayed until the sixth postoperative week. Since this precaution has been in effect, we have not experienced complications of this type. The other shortcoming of the prosthesis is troublesome rather than grave, and it consists in the tendency of the component threads of the fabric to slip and separate. Measures—chief of which is gentleness in handling—have been mentioned to prevent this mishap or to correct its consequences. This imperfection is to a large extent a manufacturing problem. Studies are now in progress to prevent its occurrence by using in the woof a Dacron yarn of different finish and much greater cohesiveness.

Results

Our clinical results so far obtained with the use of the elastic Dacron prosthesis are slightly inferior to those we achieved with homografting (Table 5). A brief reference has been already made to some of the reasons for this difference. One of the unfavorable factors of considerable importance was the prejudicial effect of case selection, the more advanced and diffuse cases having been assigned for treatment with angioplastic procedures utilizing the prosthesis. Another factor was the initial lack of full familiarity with the technical behavior of a new device. In the small series here reported, for instance, an important cause of failure was the faulty timing of angiography. It must be borne in mind, however, that, insofar as *immediate success* is concerned, a good homograft is so nearly the ideal arterial substitute that probably no plastic prosthesis will match its performance. The advantage of plastic prostheses consists in the promise that their rate of deterioration after longer follow-up

periods will be much less than that of homografts. If this is true, the late patency rate of plastic implants will be better than that of homografts, since many more of the early good results will persist. The assumption that this is what will happen is supported by excellent experimental evidence but will not be proved until the prostheses will have been observed for much longer periods of time.

Summary

An arterial substitute with elastic qualities is described. Woven of plain Dacron yarn in the woof and elasticized (Helanca) Dacron yarn in the warp as straight tubes and bifurcations, the prosthesis is seamless, smooth-walled, finely porous, light and soft, and has the ability to elongate. It is easy to procure, store, and sterilize.

In animal experiments using long aortic bypass implants, during 11 months of observation, the elastic Dacron prosthesis showed an excellent rate of patency, even when traversing a tortuous course; arteriogenesis around the implants was good and tissue reactivity low. During nine months of implantation the initial tensile strength of the prostheses was essentially unchanged. In spite of unfavorable criteria of case selection, during nine months of experience, in 43 clinical cases, the prosthesis yielded a patency rate only slightly below that obtained by us with homografts. The assumption that the *late* patency rate of these prostheses will be better than that of homografts is supported both by theoretical considerations and by experimental evidence, but it will not be proved or disproved until the results will have been followed for much longer periods of time.

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Clinical Comparison of Homografts and Braided Nylon in Arterial Bypass Surgery

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Arterial homografts were utilized in our early experience with the bypass operation for segmental occlusions. Their use involved serious problems of procurement, preparation, and storage, which led to the establishment of a blood-vessel bank.[1] As a result, the difficulties were lessened, though by no means eliminated, and initial results were satisfying.[2] Subsequently, several complications developed that were attributable to defects in the grafts themselves. Although these complications were not the main cause of graft failures, they were significant enough to cause us to switch to one of the available synthetic blood-vessel replacements. This afforded an opportunity to make a direct comparison between homografts and the synthetic vessels in similar groups of patients, largely with iliac or femoral occlusions.

Many different materials have been used for vascular prostheses by others, with varying degrees of success. Plastics have been the most promising, including Vinyon-N, nylon, Orlon, compressed polyvinyl (Ivalon), Dacron, and Teflon.[3-7] They have been used in seamed and seamless tubes prepared by weaving, braiding, or knitting. Although nylon does not now appear to be the best plastic for this purpose, it was readily available as the Edwards-Tapp [8,9] crimped nylon tube at the time we made the transition from the use of homografts to prostheses, early in 1956. The crimped nylon tube has many desirable features. It can be bent to 90 degrees without kinking, a property that is almost mandatory for successful grafting across a joint. It is elastic in length because of the braid and crimping. It is seamless and soft but does not collapse. It is fairly easy to handle, can be autoclaved, and is available in a variety of sizes and shapes, including an aortic bifurcation. Its chief disadvantage is the sometimes alarming escape of blood through its wall upon release of the occluding clamps. This is the result of the great porosity, resulting from the coarseness of the yarn and the looseness of the braid. Siliconizing and preclotting do not adequately solve this problem. However, the large size of the yarn apparently does provide an adequate margin of safety against any possible loss of tensile strength which may accrue in time from wetting of nylon.[6]

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Clinical Material

Symptomatic patients with segmental occlusions, as determined by angiography, were subjected to bypass grafting procedures. Only patients in whom at least one end-to-side anastomosis was performed are included in this study. In the present consecutive series, 56 operations were done on 45 patients. From March, 1955, to December, 1956, a total of 33 homografts were inserted in 28 patients, who comprise Group I. Group II consists of 21 patients who received 23 nylon prostheses of the Edwards-Tapp type from February, 1956, to December, 1957. Four patients had both a homograft and a nylon prosthesis and, therefore, are counted in each group. Occlusions were unilateral in 39 and bilateral in 6. All were in the iliac or femoral arteries except two, which began in the terminal aorta and extended distally. Only one patient was a woman. The age range for the homograft group was 38 to 70 years and for the

crimped nylon group, 32 to 76 years. In both groups the mean age was 60 years and the peak incidence from 55 to 65 years. The follow-up period has been 2 years to 2 years 10 months for homografts and 1 month to 2 years for nylon. Follow-up has been 100% in both groups.

Method

The technique of grafting was described by Linton[10] as the Cockett modification of Kulin's[11] end-to-side anastomosis using a homograft, and has been described by us previously.[2] The grafts were sterilized with β-propriolactone and preserved by freezing or lyophilizing. The ends of either the homograft or the prosthesis are beveled and made slightly bell-shaped for anastomosing to oval openings in the side of the host vessel proximal and distal to the occlusion with continuous over-and-over 00000 arterial silk.

The technique of inserting a nylon prosthesis is somewhat different from that of implanting a homograft. The nylon ends must be fused by heating with a cautery to prevent fraying during suturing. With homografts, when either the proximal or the distal anastomosis is completed, the other end is clamped and blood is allowed into the graft after filling it with dilute heparin solution. This permits closure of the first wound to facilitate turning the patient for the second incision when long grafts to the distal popliteal artery are necessary. Such a maneuver is impossible for the nylon prostheses because of their porous structure. The requirement of clotting in the interstices of the braided tubes to provide hemostasis precludes filling the lumen with heparin. Therefore, both anastomoses are completed before permitting blood flow into the prosthesis. When anastomosis to the popliteal artery is involved, an approach to the popliteal space from the medial side of the knee, instead of through the usual posterior incision, is helpful in avoiding the problem of turning the patient over and back again. Whereas careful preclotting with nonheparinized blood is carried out routinely, it is not as effective in controlling the initial oozing from the prosthesis as is the intermittent release of the occlusive clamps at both ends every 30 seconds until bleeding stops. This permits deposition of fibrin in the walls of the prosthesis under low pressure without allowing a long enough period of stagnation to cause thrombosis within the lumen. At present our method of preclotting consists only of coating the external surface with blood because serious difficulty with thrombosis in the lumen has resulted from internal preclotting, particularly in tubes of small diameter. Heparin in minimal amounts is used only in distal vessels to prevent clotting during performance of anastomoses.

Criteria of Success or Failure

Our postoperative evaluation has been based on rigid criteria. A graft is called a success only if proved patent by the continuous presence of a distal pulse that was absent preoperatively or by angiography or by surgical exposure. All other grafts have been termed failures. In general, we have found that subjective improvement has coincided with the patency of the graft, but clinical improvement is not included in our evaluation of success. Several patients with symptomatic improvement are included in our list of failures because the graft was not considered patent. Failures during the first 24 hours have been labeled "early," and others, "late."

Results

Table 1 summarizes the results in the entire series. Of 33 homografts (Group I) inserted, 13 (39.4%) remained patent; 11 (33.3%) were open at the time of writing, from one year two months to two years nine months. In the other two cases, the grafts were functioning at the time of

TABLE 1.—*Summary of Results in Homograft and Nylon Prosthesis Bypass Operations*

		Failure			
	Success	Early	Late	Total	Total
Homograft	13 (39.4%)	9 (27.3%)	11 (33.3%)	20 (60.6%)	33 *
Nylon	10 (43.5%)	6 (26.1%)	7 (30.4%)	13 (56.5%)	23 †
Total	23 (41.4%)	15 (26.8%)	18 (32.1%)	33 (58.9%)	56

* 33 Homografts in 28 patients.
† 23 Nylon prostheses in 21 patients.

TABLE 2.—*Causes of Graft Failure*

	Homograft			Nylon			
	Early	Late	Total	Early	Late	Total	Total
Poor run-off	8	4	12	4	3	7	19
Progression of disease		2	2		2	2	4
Rupture of graft		2	2				2
Cardiac complications		1	1	1	1	2	3
Rupture of host vessel					1	1	1
Aneurysm proximal to graft		1	1				1
Wound hematoma		1	1				1
Technical error	1		1	1		1	2
Total	9	11	20	6	7	13	33

death, from unrelated causes, three and four months postoperatively, respectively. Of the 20 (60.6%) failures in the homograft group, 9 (27.3%) occurred early and 11 (33.3%) late.

The 23 nylon prostheses (Group II) resulted in 10 (43.5%) successes; 9 of these were observed two months to one year three months. The remaining case was called successful because the graft appeared patent by arteriography, but this did not prevent an amputation two days later because of distal changes in the tissues which were not recognized as irreversible prior to insertion of the graft. There were 13 (56.5%) failures in the prosthesis group, of which 6 (26.1%) were early and 7 (30.4%) late.

The causes of failure were determined insofar as possible, and are listed in Table 2. Poor run-off was considered the cause of 12 homograft failures (60% of failures in this group), of which 8 were early and 4 late. Poor run-off was apparently the cause of seven nylon failures (54% of failures in this group), of which four were early and three late. Progression of the atherosclerotic process seemed to be the cause of two late failures in each group. Late rupture occurred in two homografts. No ruptures occurred with nylon. Cardiac complications, such as decompensation or myocardial infarction with enforced bed rest, resulted in one late homograft failure and one early and one late nylon failure. Aneurysm proximal to one homograft developed late. Rupture of the host vessel from arteritis caused by wound infection led to a late failure in one nylon case. In this case the patent prosthesis was exposed for five months in the wound, yet remained intact. Systemic heparinization caused a hematoma about one homograft that necessitated open drainage of the wound. In contrast to the durability of the nylon prosthesis in an exposed wound, the exposed homograft functioned for only two weeks, when it softened and ruptured. Harrison [12] and Scott [13] have demonstrated experimentally this superiority of a prosthesis over a homograft in the presence of infection. Technical errors related to the anastomotic surgery were considered to be the probable cause in one early failure in each group.

The slight advantage of the nylon prostheses over homografts in the number of successes will increase, we believe, as the follow-up period lengthens and the cases increase. However, there already is a definite difference in the fate of the two types of grafts.

Five homografts developed complications that were directly attributable to the grafts. On the other hand, in no case did defects in the nylon prosthesis occur. The homograft defects included rupture of the midgraft at 6 days, 11 days, and 2 weeks; severe aneurysmal dilatation at 15 months (Fig. 1), and moderate aneurysm formation at 26 months. All homograft complications but the last-mentioned have resulted in occlusion. We believe this graft, too, will become occluded eventually.

TABLE 3.—*Graft Defects*

Case No.	Homograft	Nylon
4	Postoperative hematoma with rupture of midgraft at 2 wk.	
7	Rupture of midgraft at 6 days	
12	Graft moderately aneurysmal at 26 mo.	
27	Graft severely aneurysmal at 15 mo.	
29	Rupture of midgraft at 11 days	
Total	5	0

The homograft that was aneurysmal at 15 months was removed surgically and studied. Grossly, it was sausage-like, with relatively normal areas interspersed in a series of fusiform aneurysms. The lumen was patent but was lined with thick, organized thrombus in dilated sections (Fig. 2). Microscopic examination of sections prepared with elastic-tissue stains shows fragmentation and loss of elastic fiber in dilated as compared with undilated areas (Fig. 3). Therefore, the degeneration is spotty in distribution and probably is progressive.

Examination of the failures in relation to the ages of the patients reveals only that most cases occurred during the expected peak incidence of vascular disease for both groups. Likewise, unilateral disease was not a significant factor in affecting the results.

Five patients have died. Three of these were in Group I: Two died at three and four months, respectively, of causes unrelated to the surgery, with patent grafts; one died at four months from the sequelae of a cerebrovascular accident on the day of surgery (local anesthesia), with a thrombosed graft. Two deaths occurred in Group II: One was at 5 months from rupture of the aorta at the anastomosis, with an open prosthesis; one died 12 hours postoperatively of coronary occlusion and cardiac arrest during surgery, with an open iliac prosthesis. These last two cases are counted as failures in Group II, although the prostheses were patent, because the deaths were directly related to the surgery.

Comment

Comparison of the results with homografts and with nylon prostheses in this small series of patients reveals no significant difference in the percentage of successful grafts in the two groups (39.4% and 43.5%, respectively). The shorter follow-up time for nylon does not seem to invalidate this observation, because the percentages are essentially the same if only cases followed one to two years in each group are considered (30% for homografts and 30.7% for nylon). Also, the patients in the two groups and the types of operations performed were similar.

However, a definite difference between homografts and nylon prostheses is that the late failures in the homograft group were occasionally associated with defects developing in the graft itself, whereas late failures in the nylon group were never the result of inherent defects in the prosthesis. There were five complications caused by defects peculiar to homografts and no such

Fig. 1.—Arteriogram of left femoral bypass homograft 15 months after insertion, showing marked dilatation and tortuosity.

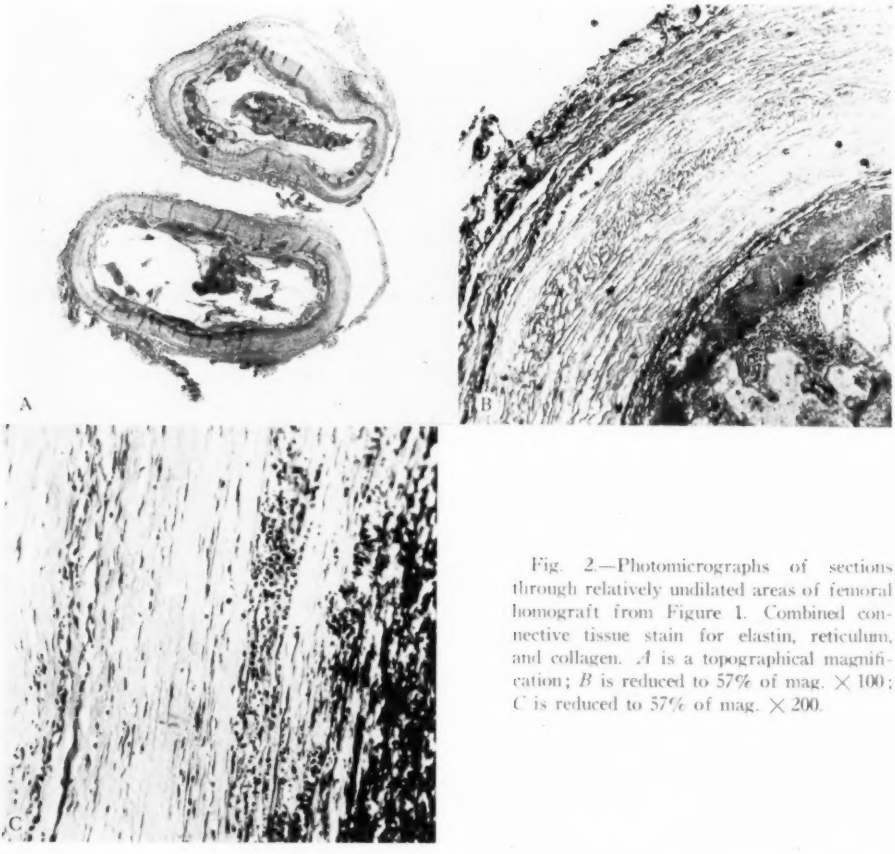

Fig. 2.—Photomicrographs of sections through relatively undilated areas of femoral homograft from Figure 1. Combined connective tissue stain for elastin, reticulum, and collagen. *A* is a topographical magnification; *B* is reduced to 57% of mag. × 100; *C* is reduced to 57% of mag. × 200.

defects in nylon tubes. This is an incidence of 15.1% in the 33 homografts used. Two of the complications probably were caused by errors in processing the graft and one by a technical error in the use of systemic anticoagulants postoperatively. The remaining two defects are more important because they are related to the inherent structure of homografts, and at the present time seem to be unavoidable. Szilagyi [14,15] has presented the degenerative changes occurring after implantation of homografts and the differences in durability among femoral, iliac, and aortic implants. Angiograms demonstrate progressive changes in aortoiliac grafts after two years and earlier and severer changes in femoral grafts. He states that after three years only a third of the latter are free of gross deterioration. It is becoming increasingly apparent that fibrous replacement of a graft by the host is slow, inconstant, and incomplete. Furthermore, after two years the amount of fibrosis seems to decrease. The muscle cells are perishable and disappear early. Thus, the long-term strength of the graft is dependent chiefly on the elastic tissue in its wall. Aortic homografts, with their high content of elastic fibers, are likely to withstand pressures better for long periods than are femoral homografts, with their muscular walls. Elastic tissue is subject to degeneration, also, as indicated by calcification and aneurysmal dilatation.[16,17] Therefore, the conclusion seems inescapable that more homografts of all types will fail from de-

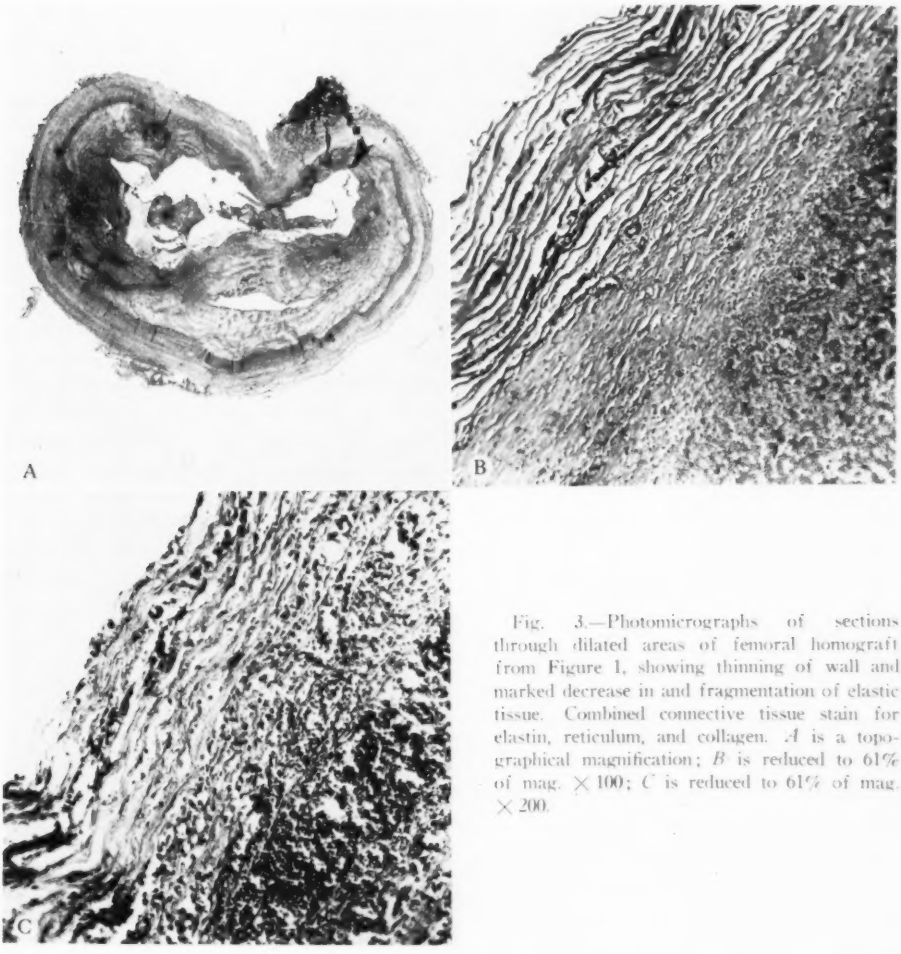

Fig. 3.—Photomicrographs of sections through dilated areas of femoral homograft from Figure 1, showing thinning of wall and marked decrease in and fragmentation of elastic tissue. Combined connective tissue stain for elastin, reticulum, and collagen. *A* is a topographical magnification; *B* is reduced to 61% of mag. × 100; *C* is reduced to 61% of mag. × 200.

terioration the longer they are followed. It becomes a question of whether degeneration of the graft or progression of the host disease occurs at the more rapid rate.

Homografts in general, then, are less durable than plastic tubes. Nylon, as used in this study, has shown no tendency toward weakness for periods up to two years. When examined after late failure from other causes, the nylon has been in good condition. It seems likely that it will outlast the patient in most cases. Furthermore, new materials, such as Teflon, which is practically indestructable, remove any question of durability. Crimped Teflon, only recently available, will probably replace crimped nylon tubes because of its several advantages.[6,12,18,19]

Although the ideal prosthesis has not been developed as yet, the nylon tubes used by us have eliminated an important cause of graft failures from defects in the structure of the graft itself. More failures from longer follow-up periods are most likely to be the result of changing conditions in the host, such as progression of atherosclerosis with decrease in the distal run-off or proximal inflow. The results in this

TABLE 4.—*Deaths*

Case No.	Time After Operation	Cause	Condition of Graft: Homograft	Condition of Graft: Nylon
14	4 mo.	Unrelated	Open	..
19	3 mo.	Unrelated	Open	..
23	4 mo.	Sequelae of cerebrovascular accident on day of operation	Closed	..
53	4 mo.	Rupture of aorta at anastomosis	..	Open
56	12 hr.	Cardiac arrest and coronary occlusion at operation	..	Open

small series suggest that homografts are inferior to plastic prostheses.

Of course, there are other factors in maintaining patency more important than the type of graft used. The most critical of these is an adequate distal run-off. Nearly every writer on the subject has emphasized this point, Deterling[20] perhaps most recently. Careful selection of patients, with insertion of grafts only in the most suitable, is the best way to improve over-all results. Our experience certainly confirms this observation. Meticulous attention to technical details is absolutely essential, as stressed by Pratt.[21] Sufficient skill should be developed in the dog laboratory if clinical experience is limited. The type of surgical procedure employed is important, and the bypass method enjoys current favor.[2,7,8,10,11,20] Strict asepsis must be enforced to prevent the catastrophe of a wound infection in the presence of a foreign body. When this occurs, adequate surgical drainage combined with the indicated antibiotic therapy must be vigorously applied if the graft is to be salvaged.[12,13] Whether or not endarterectomy[22] can be improved and used to extend the application of grafts is not clear at present. Our experience with it has been uniformly bad. As far as homografts are concerned, it may be possible to improve the results from their use by better methods of sterilization[10] and by using vessels with relatively high elastic tissue content as grafts.[14,15,17] For small-vessel grafts, there may be some advantage in the use of fresh homografts.[23] However, we are inclined to believe that the day of homografts is drawing to a close unless the problems of tissue specificity and of atherosclerosis in the graft can be solved.

Summary

A group of 33 femoral and iliofemoral homografts were compared with a group of 23 Edwards-Tapp nylon prostheses in a series of 45 patients with bypass procedures. The results with the two types of grafts were similar except in one important respect: Five complications resulted from defects in homografts, of which three were ruptures and two were aneurysms; no defects were observed in the nylon tubes. These defects result in graft failures and present a point of attack to improve the results of bypass surgery. Plastic devices for blood-vessel replacement have not been perfected, but it appears that some of them already are superior to homografts.

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DISCUSSION

ON PAPERS BY DRS. SZILAGYI, FRANCE, SMITH, and WHITCOMB, and BY DRS. HOHF, TRIPPEL, and LAUFMAN.

DR. OTTO H. TRIPPEL, Chicago: There is one important detail that probably deserves emphasis here which is indirectly pertinent to the main purpose of this paper. The detail is this:

Although it appears that approximately 60% of these grafts ended in being listed as failures, it should be remembered that an appreciable percentage of these so-called failures are and should be classified as temporary successes. Some grafts remained open for periods of 6 to 18 months before undergoing occlusion and finally entered the category of failures.

Thus, even though ultimate occlusion of these arterial prostheses is a real probability, their palliative value in returning patients to temporary rehabilitation or useful employment must be considered.

DR. WILLIAM S. DYE, Chicago: We are now using a crimped Dacron prosthesis for femoral bypasses, and they are proving very satisfactory. Autogenous vein grafts may be used with success provided the size is adequate. Our longest period of follow-up is with autogenous vein grafts. Six cases have been followed for seven years and five cases from five to six years.

We have also had aneurysmal dilatation in vein homografts. These grafts were fresh homografts, and so the aneurysm was related to the type of graft rather than to their preparation.

DR. D. EMERICK SZILAGYI, Detroit: I will divide my remarks into two parts. First, I would like to discuss Dr. Laufman's paper; he kindly asked me to do so.

It is most gratifying that the observations on the biologic fate of human arterial homografts which we reported a year ago are confirmed by the careful work of Dr. Laufman and his associates. The opinions regarding the behavior of arterial homografts are, however, far from unanimous. Many excellent surgeons still feel that the lasting qualities of arterial homografts are satisfactory. We need, therefore, a greater accumulation of postoperative observations and, in particular, angiographic observations, since the clinical appearances of cases with arterial grafts are often unrevealing with respect to the state of preservation of the implants. We are in especially urgent need of such post-

operative angiographic studies from workers who used or are using sterilizing methods different from ours, because the notion has been advanced that degenerative changes such as my associates and I described may be due to the effects of the sterilizing agent β-propiolactone. The findings of Dr. Laufman and his associates do not strengthen our own case in this regard, since their sterilizing method was the same as ours. It would be most desirable to see the results of long-term angiographic follow-up studies on groups of patients whose implants had been sterilized with ethylene oxide and other agents. I expect that such grafts will show essentially the same changes as our own do, since in my opinion the degenerative changes are brought about by immunological factors rather than by any assumed damage in processing.

With regard to our own presentation, I should like to state very briefly the qualities for which we were looking in our search for a serviceable plastic prosthesis. The prosthesis we sought had to be nonreactive, durable, and of a construction that would allow good arterial regeneration and present optimal hemodynamic conditions; there were, of course, also some considerations of practical importance, such as the handling quality and the ease of the sterilization, as well as that of cost.

We believe that the prosthesis we have just described comes close to meeting many of these requirements. Needless to say, one important question regarding its performance, that of its durability or staying power, will not be answered until our follow-up observations extend over a longer period of time. On the grounds of experimental observations, we strongly feel that the lasting quality of the prosthesis will be good. I should like to interject the comment here that in our tabulation of the results the word "late" is used in a rather loose sense. It refers merely to the cumulative assessment of the state of the implants any time after discharge from the hospital. In the true sense of the term, "late results" should refer to implants at least two years old.

I should like to point out that the pseudointima of this prosthesis is rather slow in developing. For this reason, postoperative angiographic examinations ought not to be performed in cases with this type of implant in less than six weeks after operation.

A word of caution would be in order as regards the technical aspects of the use of plastic fabrics in arterial surgery. The woven tubes require a degree of familiarity with their handling qualities that is acquired only through experience. The best place to acquire this experience is in the animal laboratory.

DR. HAROLD LAUFMAN, Chicago: I would like to make just two brief points.

First, we need to have a new classification for judging results of blood vessel grafting. I think we must judge results in terms of one-year successes, two-year successes, and so on, pretty much in the way we do with carcinoma surgery, and not in terms of total success or failure.

Second, I do not believe we have the ideal blood-vessel substitute yet, whether it be a homograft or a vein or an artificial substance. I believe the all-too-comforting thought that if we do not have a very good artificial graft we can always use a homograft, is erroneous. Homografts themselves are far from perfect in a permanent sense. But I believe more research of the type Dr. Szilagyi and others are doing will eventually give us something that will be more universally useful.

The Treatment of Postmastectomy Lymphedema

BROCK E. BRUSH, M.D.; JOHN H. WYLIE, M.D.; JOSEPH BENINSON, M.D.; MELVIN A. BLOCK, M.D., and THOMAS J. HELDT, M.D., Detroit

Swelling of the arm following radical mastectomy may become severe, painful, and quite disabling. The problem has been with us since the beginning of radical breast surgery. It was thoroughly studied by Halsted,[1] and his observations and opinions on the subject remain a classic to this day. He observed that in many instances, a year or more following the operation and without return of the disease, there would occur sudden or gradual swelling of the upper extremity. Halsted also studied patients with swelling of the arm in whom no surgery had been done, as well as those in whom late postoperative swelling accompanied a recurrence of the disease. In many instances when Halsted removed the axillary and supraclavicular nodes and resected a portion of the subclavian and axillary veins, no edema of the arm developed. He further observed that less difficulty occurred after skin grafting than after some plastic closures.

Halsted concluded that infection was "a very frequent if not indeed usually the overlying cause of swelling of the arms whose main lymphatic channels have been more or less blocked by operation." This infection he stated may be so mild as to escape the observation of even those intently on the lookout for it.

Veal[2] showed by phlebograms that angulation of the axillary vein often occurred, and he believed that the venous return was the important factor in etiology, whereas Foley's[3] studies disputed this idea. Drury and Jones[4] demonstrated that edema was quite likely to follow a maintained increase in venous pressure, and Parker, Russo, and Darrow[5] found a correlation between the development of lymphedema and obstruction of the main venous channels. Lobb and Harkins[6] studied the total problem and found that excision of a segment of the axillary vein did not markedly influence the number of patients who developed edema, or the severity of it. In their series infection did not seem to be as important an etiological factor as it had previously been considered to be.

Wakim, Martin, and Krusen[7] showed that chronic edema results in changes in the subcutaneous tissues toward induration, thickening, and fibrosis and advocated early treatment by centripetal rhythmic compression of the edematous limb for one-half hour twice daily. They demonstrated that the edema and pain could be relieved and the color and consistency of the skin would become more normal. The basis of improvement they felt was a regeneration of lymphatic connections, reestablishment of collateral blood vessels, and development of new avenues for both lymph and blood.

Reichert[8] demonstrated the importance of the regenerating lymphatics in aiding the veins to overcome edema and to restore a more normal state.

The role of postoperative roentgenotherapy has been discussed by Holman, McSwain, and Beal,[9] and, in addition, the aspect of the presence of axillary metastases at the time of surgery.

One of the most distressing features of an edematous arm is the frequent recurrence of infection, as demonstrated by chills, fever, and localized redness and pain. The relief from these episodes has been one of the most gratifying aspects of treatments

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which reduce the edema and return the arm to a more normal state.

Prevention

Since infection is one of the important causal factors of later trouble, the prevention of postoperative fluid collections is all-important. The use of constant suction drainage for several days by the insertion of catheters at the conclusion of the operation, as advocated by MacDonald and Osman,[10] has resulted in much less infection and improved healing of the skin flaps. Fitts, Keuhnelian, Ravdin, and Schor[11] studied the etiology of arm edema following mastectomy and could find no one determining factor. The number of nodes removed, obesity, and necrosis of skin edges were studied, as well as postoperative fever, fluid collection, and infection. Prophylactic penicillin did not appear to be beneficial in preventing edema incidence.

Early arm exercises leading to free and complete mobility of the arm and shoulder have long been stressed as an important step in the avoidance of later arm troubles.

A skin graft should be employed whenever there is any tightness of the skin flaps. The skin graft is much preferable to any plastic procedure on the skin, and an adequate skin graft will result in a much greater freedom of motion.[12] Arm exercises should be begun in the immediate postoperative period and continued for at least six months. They should be such as to promote free and complete mobility of the arm, including reaching behind the head and reaching to a vertical position. While such exercise often gives some discomfort in the early stages, the results of a determined exercise program are indeed worth the effort.

Elastic arm bandages for the first six months following the operation have been advocated and would seem to have merit. It has been shown that when the venous pressure gradually increases in the postoperative period edema is likely to follow. The inconvenience of using these bandages is well repaid in later years. We have not used them in a preventive way.

The fixation of the skin flaps, as advocated by Larsen and Hugan,[13] should result in less fluid collection and better healing of the incision.

Method

The apparatus which we have utilized is comprised of three features: 1. A sleeve of special fabric in the length of which are incorporated two inflatable rubber tubes of about 1-in. caliber. This sleeve is laced on so that it can be adjusted to an arm of any size. A nonelastic glove is used in conjunction with the sleeve to prevent swelling of the hand while the pump is in use. 2. A specially constructed, electrically operated air pump with a timing device permitting inflation of the rubber tubes for 15 seconds and a collapsing rest of these tubes for 45 seconds of every minute that the device is in operation (Fig. 1). 3. A custom-measured pressure-gradient sleeve to be worn when the pump is not in use.* The arm measurements for this sleeve are taken after a few days of pumping, when the arm has been reduced in size.

It has been our practice to begin the treatment with three to four days of rather intensive pumping. Most patients will tolerate the pump for periods of six to eight hours a day. As the arm diminishes in size, the sleeve is tightened every two to three hours. When the arm has been reduced to near-normal size, the sleeve is laced less tightly. After several days the arm is measured for an elastic sleeve (Figs. 2 and 3). The pumping device is reapplied at intervals of a few days to a week or two and permitted to operate for several hours, as needed to reduce accumulated swelling.

* The sleeve and pump are supplied by the Jobst Institute, Toledo, Ohio.

Figure 1

Figure 2

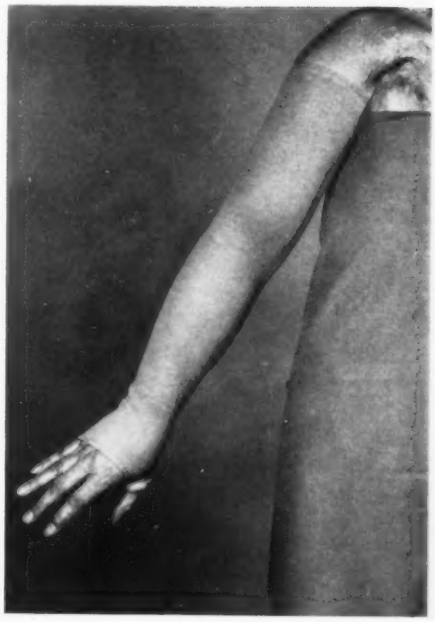

Figure 3

The apparatus, after an initial period of treatment and instruction, is used at home under medical supervision. Since our original report,[14] a new pump has been developed after a pilot model made by the Scientific Laboratory of the Ford Motor Company. The new pump weighs 15 lb. and can be taken on trips, vacation, etc.

The device must be used under the supervision of a physician. A thorough understanding of the objectives by the patient leads to better cooperation and thus a more satisfactory result. If there is evidence of local axillary and lung metastases, we have relied more on the sleeve and less on the pump. The use of a custom-made sleeve for periods when the pump is not in use is an essential part of the management.

The following instructions are posted inside the cover of each pump:

1. Use only under medical supervision.
2. Stop the pump for 15 minutes every 2 hours.
3. Do not lace the sleeve too tightly at the end of the treatments when the arm is near normal size.
4. Discontinue the pump if the patient experiences any significant distress in the arm.
5. Do not expect a large, long-swollen arm to be reduced by the first treatment.
6. Do not use the pump when there is evidence of lymphangitis.

A tracing of the pressure curve is shown in Figure 4.

Results

We have treated 32 patients who had severe and disabling edema of the arm following radical mastectomy, with heartening results. Significant relief has been obtained in all patients except two, who were in the late stages of generalized cancer and did not tolerate the device. In many instances when the edema was of long standing (seven or eight years), the results were surprisingly good.

Illustrative Case Reports

Case 1.—A 64-year-old white woman had a radical mastectomy in November, 1956, for carcinoma of the left breast. Axillary lymph nodes were involved with metastatic tumor. Her wound healed primarily, and she received a course of radiotherapy postoperatively. Approximately five months following surgery there was severe swelling of the entire left upper extremity. She was treated with the pressure sleeve for three days, with 2 to 2½ in. reduction in the circumference of her arm and forearm. Following this she was fitted with an elastic sleeve, and the swelling has not returned

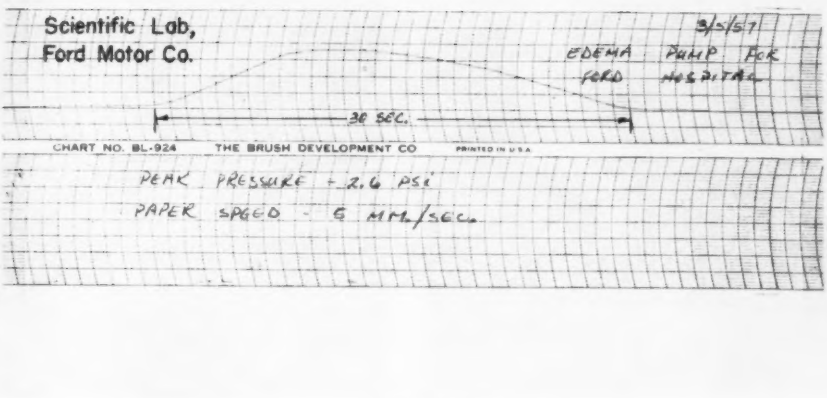

Figure 4

to any significant degree. She has good use of the arm and has no discomfort.

Case 2.—A 72-year-old white woman had a left radical mastectomy for carcinoma of the breast in 1933. For approximately 15 years prior to her admission here she had edema of the left arm and forearm to such a degree that any significant use of the arm was impossible. The edema at times became so severe that she could not hold the arm up because of its weight, and her discomfort and disability were great as a result of this excess weight. Her arm and forearm were between 5 and 6 in. greater in diameter than the opposite normal arm. Decompression was first started January, 1958, by simply wrapping the entire arm from fingers to axilla in elastic bandages. After partial decompression in this manner, the pressure sleeve was applied and used intermittently for five days. The arm and forearm were reduced in circumference by approximately 4 in. She now wears an elastic sleeve, which maintains about 75% of the decompression originally obtained. She will undoubtedly improve further with repeated treatments with the compression pump.

This reduction in the size of her arm has again given her a useful arm and has made it possible for her to wear long-sleeved garments without any alterations, and the fatigue resulting from the heavy, edematous arm has been almost eliminated.

Case 3.—A 55-year-old white woman had a left radical mastectomy for carcinoma of the breast in 1942. Beginning six weeks after the surgery, there was generalized lymphedema of the entire left arm, which had gradually become worse over the years. In January, 1956, she was treated with the pressure pump and sleeve, and the swelling in the arm and forearm was reduced 3 to 4 in. She continued to use the pump at home with gradually diminishing frequency, and now uses it only about once a month. She wears the sleeve every day. She writes: "I have absolutely no pain or heaviness in the arm and very little swelling. When we go out in the evening, I remove the elastic sleeve, and I can wear a much shorter dress sleeve than formerly. A new elastic sleeve is ordered about every three months."

Case 4.—A 60-year-old white woman had a left radical mastectomy for carcinoma of the left breast in October, 1956. The axillary lymph nodes were involved with metastatic tumor. Postoperatively she had a moderately severe wound infection and required skin grafting to complete healing of the wound.

She received a course of deep x-ray therapy.

Approximately six months after surgery there was moderately severe swelling of the entire forearm, arm, and shoulder. The arm became very tense and almost unusable, with intense pain at times. She was treated with the pressure sleeve for five days, with reduction of 2 to 3 in. in the circumference of the arm and forearm. This practically eliminated the pain and gave her nearly full range of motion. She was fitted with an elastic sleeve, which she wears continuously except at night. Five months later she has full use of her arm; it is nearly normal in size and is not at all painful.

Case 5.—A 60-year-old white schoolteacher had a right radical mastectomy in 1952. Shortly after surgery her arm became swollen to approximately

twice its normal size. Her arm became useless and disabling and almost eliminated her from her profession. She was treated with the pressure sleeve in July, 1957, and the arm and forearm were reduced in size by approximately 1½ to 2 in. She now wears an elastic sleeve, and she carries on a full teaching schedule.

Before her treatments she had frequent episodes of lymphangitis with chills, fever, and general malaise. Since she has been wearing the sleeve, she has not had a single episode of this kind.

Comment

While the factors affecting the flow of lymph have been studied for over 100 years, some features of lymph propulsion still remain uncertain. Starling[15] early established the fact that massage and exercise greatly increase the flow of lymph. While arm elevation, massage, brachial-plexus block, and other forms of treatment have been of benefit, the device here described has been much more satisfactory in our hands.

The exuberant comments of the patients who had suffered from severe edema for many years have been very gratifying. The relief from the discomfort and pain has been the result which most patients have stressed. The distress from a huge, swollen arm results from the increased weight, sensory disturbances in the skin, stiffness, and reduced mobility of the whole extremity, including the hand and fingers. The pain in most instances has seemed to be due to the tension in the arm, as exhibited by the hardness. The relief of pain occurs as the arm softens and the tension is decreased. It soon became evident that a great deal of relief was obtained when the arm was only partially reduced in size.

As has previously been described, the return of the arm to a more normal state has resulted in a greatly decreased incidence of attacks of lymphangitis and cellulitis.

The relief of edema has enabled many patients to wear clothes without expensive alterations. The boost to morale has been most interesting to watch in many instances. The relief from the embarrassment of a swollen arm has resulted in many of these patients again leading a normal life. They have resumed social functions and have returned to their former place in community life.

The fear of deformity has been a factor deterring some patients from accepting the ideal procedure for cancer of the breast. This fear of disability can be minimized if edema can be successfully treated.

After the initial period of treatment and instruction, additional treatments are carried out in the home. The need for further use of the pump, after the initial course of treatment, has been quite variable. One patient uses the pump for a few hours every three weeks, while several other patients require only their elastic sleeve. For the most part, the sleeves are removed at night and put on each morning. Several patients, after a few months of treatment, have discontinued even the use of the sleeve. With ordinary use the sleeves remain in good condition for three to four months. The importance of a custom-measured sleeve cannot be overemphasized.

Summary and Conclusions

Edema of the arm may be successfully treated by means of an appliance to reduce the swelling, plus the use of a custom-fitted sleeve when the pump is not in use or no longer needed.

The pain, discomfort, and swelling are relieved.

The incidence of chills, fever, and localized infection is greatly diminished.

Strict adherence to instructions is important, and medical supervision of the device is imperative.

Swollen arm, a troublesome sequela of radical breast surgery, need not be tolerated.

Henry Ford Hospital.

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DISCUSSION

DR. W. ANDREW DALE, Rochester, N. Y.: We are in the process of evaluating this device, as well as a similar one; and, because this apparatus has been so well shown by Dr. Brush, I would like to show two slides of a similar outfit, emphasizing that I have no stock in either one. We at the Strong Memorial Hospital are primarily interested in determining which, if either, has an advantage over the other.

(Slide) This device was made by a dentist, Dr. Weinberg, on Long Island. He tells me he made it because his wife had postoperative edema of the arm. It has subsequently been modified here, as you see, to handle a leg.

(Slide) The only difference in this gadget is that there are a series of air-containing cells which are actuated to the present pressure at 15-second intervals; it has, therefore, been characterized as a milking machine in that it tends to milk the edema fluid up the arm or up the leg.

So far I am most impressed by what the patients have told me. They say they are very happy with the machine, that the arm is considerably freer of pain, and that they can use the arm better.

I think the custom-made stocking which Dr. Brush has presented is probably just as important as gadgets to reduce the edema initially, if not more so.

DR. RUSSELL L. MUSTARD, Battle Creek, Mich.: Up to 17 years ago I thought I didn't do a decent job on a radical amputation of the breast unless I uncovered the axillary vein right down to its very thin blue wall. I was getting a tremendous percentage of these horribly troublesome lymphedemas of the arm, and one or two of them were so bad that the poor souls had to carry their arms in slings.

I reasoned on two grounds: First, we were seeing metastases into the axilla and supraclavicular areas infrequently. The metastases were more apt to be distal into the bones, lungs, and mediastinal areas. Second, a great deal of the lymphatic supply of the extremities travels in the adventitia and areolar tissue around the axillary vein, and so I attempted a small individual experiment.

Seventeen years ago I started doing the typical radical breast operation that all of us do, with the one exception that I stopped dissecting that vein down to the thin blue wall. I have left the adventia and the areolar tissue around the vein. I have dissected out all of the nodes, all of the muscles, all of the breast, and a wide area of the skin, and I see that there is complete hemostasis, but I have not gone down to that thin blue vein wall for the past 17 years. As a result, lymphedema has ceased completely to be a problem with me. In an occasional case there may be the faintest amount of swelling in the arm, but massive lymphedema has completely ceased to be a problem, as far as I am concerned.

What has this done to my survival rates? It has not changed them one bit. Roughly, the five-year survival rates were around 34% when there was axillary involvement and 78% where there was no lymph node involvement. Those are my

rates today—17 years after initiating my little experiment.

Therefore I am very strongly of the belief that the terrific lymphedema that comes into the arm in these particular cases is almost entirely due to our removal of the very thin layer of areolar and adventitial tissue around the vein. In my experience, by leaving that thin layer in place, I have not increased the morbidity or the death rate of these patients at all.

DR. BERNARD B. LARSEN, Cleveland: I should like to compliment Dr. Brush on working out something that will help these distressed patients.

My experience has been somewhat like Dr. Mustard's. Since I have been using the tacking-down technique on skin flaps (you will recall that my paper was presented here in 1955, and this series has now grown to 65 patients, or, rather, 65 radical mastectomies in 64 patients), in no case has there been over a ½ in. increase in the circumference of the arm, except for patients who were treated postoperatively with x-rays. I believe that with a careful surgical technique in closing the axilla with a skin flap tacked down so as to get primary healing, and avoidance of drainage of these wounds by either soft-tissue drains or any other method, the incidence of lymphedema will be cut down considerably.

Another thing we should consider is just how many of these patients should have x-ray therapy. I should like to repeat that the ones without x-ray therapy have presented no problem. This is not true after intensive x-ray therapy following radical mastectomy.

DR. BROCK E. BRUSH, Detroit: I wish to thank Dr. Dale for his discussion. His device, which we have known something about, is, I am sure, just as efficient as ours. I do not know the relative costs. We must use some device which is reasonable in price, efficient, and portable so that it may be used by the patient at home under medical supervision. The main thing is to use some device which will pump down the edema and then use a sleeve which will keep it down. We feel that the sleeve must be custom-made and of a pressure-gradient type. We have been very pleased with our results when both the pump and the sleeve are used.

Dr. Mustard has made an interesting observation. Every feature of the condition, such as the removal of an axillary vein segment, removal of the supraclavicular nodes, involvement of the axillary glands, and infection, has been studied. These factors have been evaluated in several series, and it seems difficult to incriminate any one etiologic feature.

I do know that most of these patients whom we have treated, who have come from various places, have had x-ray therapy, and sometimes they have seemed to have quite a bit of it. It has been our policy to use x-ray therapy on patients who have positive axillary glands at the time of the radical breast operation, since it has been proved worth while in our experience. I believe that when a patient has positive nodes at the time of the radical breast operation, she should be given x-ray therapy; and if edema develops later, this device can be used to control it. I believe that nothing less than a classical radical operation should be done.

I am familiar with Dr. Larsen's work. We have used this technique and have also used suction tubes under the skin flaps. I believe it is very important to prevent fluid collections under the flaps.

The Peripheral Venous Heart

JOHN McLACHLIN, M.D., and ANGUS D. McLACHLIN, M.D., London, Ont., Canada

Pulmonary embolism is now the commonest single cause of death following major surgical procedures. Bell and associates [1] reported 51 deaths in 901 patients who had had operations for cancer of the colon or rectum. Eighteen, or about one-third of these deaths, were attributed to pulmonary embolism. Three of the ten deaths in Hughes' [2] series of 227 combined synchronous abdominal-perineal resections of the rectum were due to pulmonary embolism, and other reports confirm the finding that about one-third of the postoperative deaths in major surgery are a direct result of this distressing complication.

We [3] believe that venous stasis in the lower extremities is the prime factor in venous thrombosis and subsequent pulmonary embolism. This led us to a study of the pump mechanism, or "peripheral venous heart," in the calf muscles with the hope of finding a means to control venous stasis.

It is still unsettled whether thrombi arise more commonly in the calf veins or in the veins of the thigh and pelvis. Gibbs [4] reported that the calf muscles were the commonest site of thrombosis but that most emboli originated in the thigh or pelvis. We [5] found that 73% of thrombi began in thigh or pelvic veins and that 56% of these subjects had an associated pulmonary embolus. Thrombosis in the thigh and pelvic veins thus seems more likely to produce embolism than a similar process in the calf. Irrespective of the site of the venous thrombosis, the venous pump in the calf muscles should be capable of increasing flow in the calf, the thigh, and the pelvic veins and so lessening the danger of thrombosis.

The arrangement of veins and muscles in the calf is ideally suited to drive venous blood in a proximal direction.

The rigid interosseus membrane in front of the soleus muscle and the strong fibrous capsule around the calf muscles ensure that contraction of the calf will have a pumping action on these veins. In the normal leg, valves will prevent distal flow and consequently blood will be forced toward the heart. When the muscle relaxes, blood fills the vein from below and the process can be repeated. Postural muscle tone, with its alternate contraction and relaxation of muscle groups, will have a similar, but much less marked, effect when the leg is at rest.

We have studied venous flow in normal legs in patients undergoing intravenous pyelography. A blood pressure cuff applied just above the malleoli at 80 mm. pressure will direct diatrizoate (Hypaque) injected through a superficial vein on the dorsum of the foot into the deep veins of the leg. Fifteen cubic centimeters can be injected in five seconds, and, if the leg be kept at rest in a horizontal position, enough dye remains in the deep veins of the calf to be visible on x-ray examination as long as five minutes after the injection.

A much clearer and more graphic concept is obtained by cineradiographic studies. With this aid, blood, as outlined by the radiopaque dye, is seen actually squirting out of the veins in and about the soleus muscle with each contraction of the calf muscles and can be followed as stream lines (Franklin and McLachlin [6]) up into the popliteal vein. The process is readily appreciated in a moving picture but, unfortunately, cannot be reproduced in this paper.

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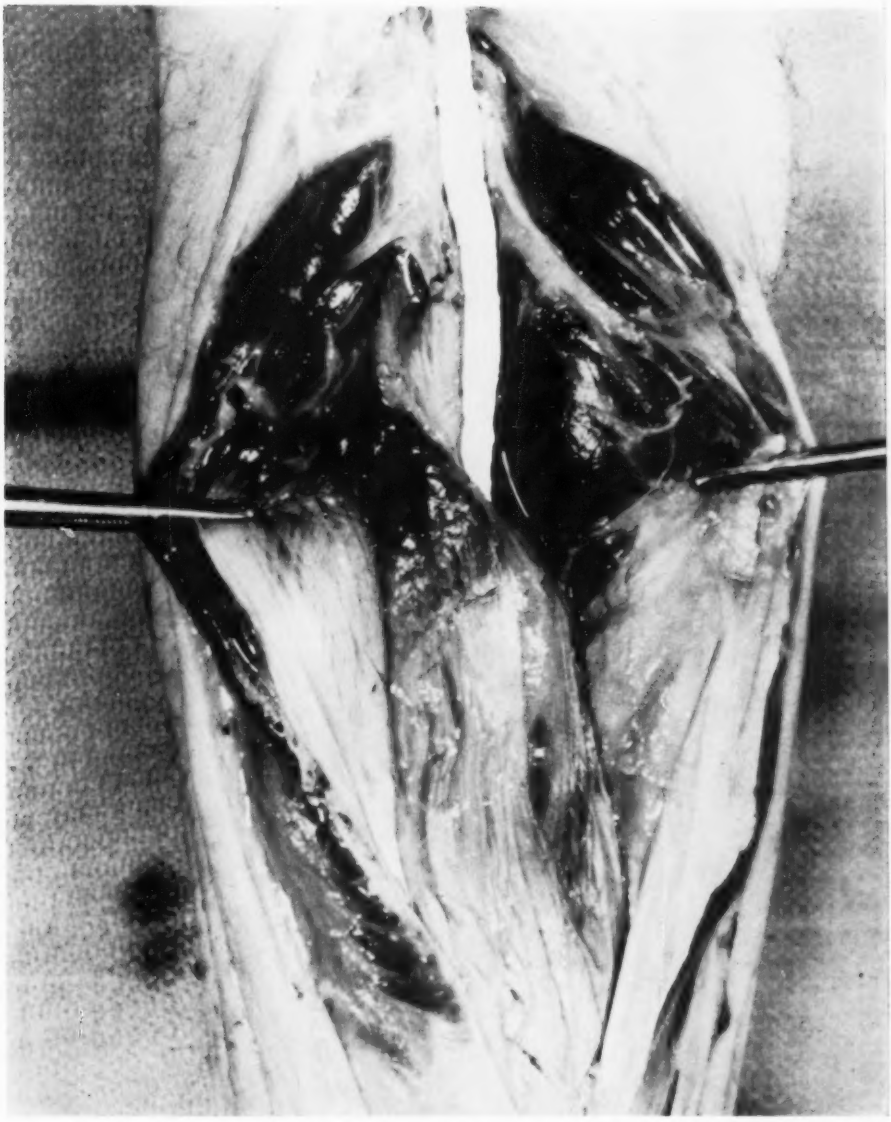

Fig. 1.—Anatomical dissection showing the popliteal vein emerging from the upper edge of the soleus muscle. The vein in the print has been painted for better demonstration.

The long delay in emptying the deep veins of the leg suggested that even in healthy patients there is only a narrow margin between movement and stasis in the veins of the lower extremity. When movement in the leg muscles is reduced by putting the patient to bed, or even further reduced by an anesthetic and the postoperative period, stasis is inevitable and thrombosis may readily begin. Learmonth and Slessor [7] found that paresis of the calf muscles produced by neurectomy in the

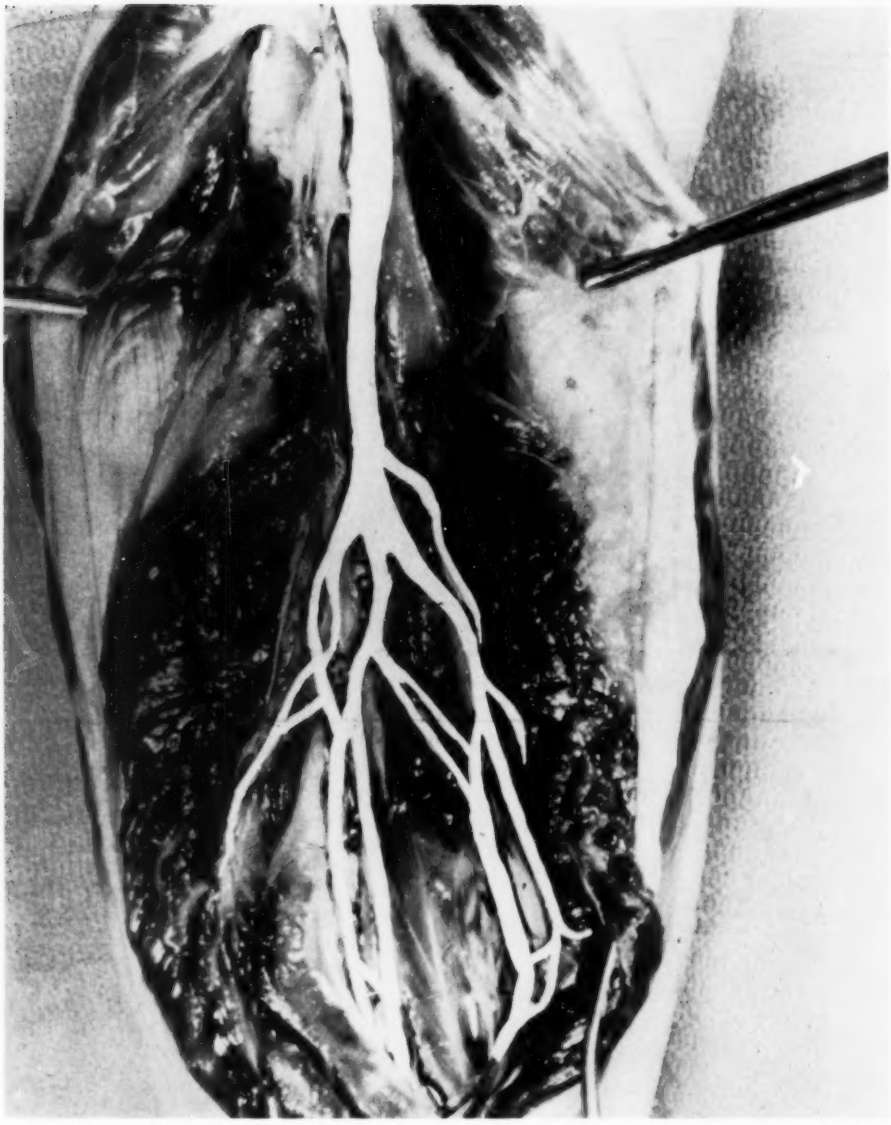

Fig. 2.—The vein is formed by junction of a large number of tributaries from the belly of the soleus muscle or on its anterior surface.

treatment of intermittent claudication favored stagnation and thrombosis in the paralyzed muscles. Smirk [8] found that exercise decreased the venous pressure in the foot veins and believed this to be due to the pumping action of the leg muscles. Breathing had very little effect on the pressure in the foot veins.

With this evidence that the calf muscles are capable of maintaining blood flow in the leg veins and our belief that stasis is the precipitating factor in venous throm-

Fig. 3.—Photograph, made during use of a rapid cassette changer, shows a decrease in amount of dye in the deep veins of the calf following a single electrical stimulation of the calf muscles.

bosis, it seemed logical to keep the calf muscles contracting, that is, "keep the patient walking while being operated on." We have used skin electrodes similar to those employed in electrocardiography. One electrode is applied over the upper inner aspect of the calf and the other over the inner side of the Achilles tendon. Direct muscle stimulation will now produce contraction in the calf muscles of the anesthetized patient. When curare-like drugs are used, a greater length and strength of stimulus may be required. With a set interval between stimulations and a set duration of the stimulus, the voltage is adjusted to give an adequate contraction in the calf muscles of that person. The electrical circuit is closed and explosion-proof and will now produce regular contractions in the calf muscles during the operative period and until the patient is conscious enough to move about. We are still determining the length and type of stimulus that will most closely approximate the normal pumping effect of the calf muscles. There seems no doubt that blood can be kept moving in the legs in this physiological manner.

The apparatus is simple, easy to apply, and does not disturb the operating room. Only time and an adequate number of cases will let us determine whether keeping the peripheral venous heart active during operative procedures will lessen the frequency of pulmonary embolism.

While primarily interested in the pumping mechanism of the calf muscles, we have used the rapid cassette changer and cineradiography to study the effects of breathing on venous flow in the legs. It has long been recognized that inspiration causes col-

lapse of the neck veins, while expiration makes them distend. This seems good evidence that inspiration increases venous return from the head and upper extremities. The concept is not necessarily true in the lower extremities. Descent of the diaphragm, while increasing negative pressure in the thorax, also increases intra-abdominal pressure and interferes with venous return from the legs. The same impairment of venous return is seen in the patient with a distended abdomen. Franklin [9] stated that variations in venous return, unless temporary in character, can be produced only by variations in peripheral inflow, and there is no evidence that the last is seriously influenced by respiratory movements. In the intact experimental animal, the nonhepatic abdominal inflow into the thorax tends to be held up, or even at times reversed, during inspiration. In addition, the valves in the femoral veins do not close during inspiration, and an increase in intra-abdominal pressure caused by descent of the diaphragm may well force blood back into the leg veins.

Our own observations of flow in leg veins using the rapid cassette changer and cineradiography do not show any appreciable increase in rate of flow even on deep breathing.

Cineradiography was once again very convincing in showing no appreciable movement of the dye even on forceful respiratory movements, while contraction of the calf muscles produced the obvious emptying effect described above.

Two other factors in venous return must be mentioned. Left ventricular vis-a-tergo implies that the force initially applied by the left ventricle, while dissipated by passage of blood through the arterioles and capillary bed, still persists into the venous system. Best and Taylor [10] state that in the

Fig. 4.—On the left, the deep veins of the leg are well outlined with dye. In the middle, the dye is still present even after three deep breaths. On the right, the deep veins have been almost completely emptied by a forceful contraction of the calf muscles.

leg veins the pressure is still 20 cm. of water, and in the right auricle, about 0.5 cm. of water. Arteriovenous shunts, permitting a direct transfer of arterial pressure into the venous system, may also be a factor in venous flow but are as yet poorly understood.

From our own observations we believe that muscle action, and in particular the peripheral venous heart in the soleus muscle, is responsible in good part for return of blood from the legs. If stasis in the leg veins is the precipitating factor in venous thrombosis and subsequent embolism, it seems logical to keep blood moving in the legs by electrical stimulation of the calf muscles during the otherwise enforced idleness of an operative procedure and the recovery period.

Summary

We have used anatomical dissection and x-ray studies with a rapid cassette changer and a cinecamera to study the soleus pump, or "peripheral venous heart," in the calf muscles.

The pumping action of the calf muscles has been demonstrated. Respiratory movements have no appreciable effect on venous flow in the legs.

Electrical stimulation of the calf muscles during operative procedures is suggested as a means of preventing the venous stasis in the legs that we believe is the precipitating factor in venous thrombosis and embolism.

Dr. G. G. Copestake gave radiological assistance in this work.

Dept. of Surgery, University of Western Ontario Faculty of Medicine.

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DISCUSSION

DR. HARRY H. MCCARTHY, Omaha: Dr. McLachlin has asked me to discuss his presentation. At the same time, I would like to say just a word about Dr. Brush's work. Rather than get up twice in succession, I thought I would discuss the two concurrently.

Since 1948 I have been interested in this problem, feeling that the pressure ischemia and lack of muscular activity in the legs of the patient on the operating table is a major factor in the production of postoperative thrombi and emboli, thrombophlebitis, and pulmonary emboli. The pooling of the blood in the legs and the lack of muscular activity are extremely dangerous.

We have used a pump with rubber boots covering the leg up to the knee, enclosing the foot. A small pump propelled by compressed air is used to obtain cyclic systolic and diastolic pressures, and thus we have been able to simulate the action that Dr. McLachlin has pointed out here. The cycles may be four or five a minute, but can be adjusted to any number. We feel it is rather effective in returning blood to the heart.

Gravity and negative intrathoracic pressure, muscular activity, and lack of venous obstruction are the four factors that help blood return to the heart and prevent pooling in the legs. In many cases gravity and lack of muscular action are detrimental to the patient who is on the operating table.

It is particularly important that, owing to the anatomical fact that the lesser saphenous vein enters the popliteal at a very acute angle, the acuteness of the angle is increased by pressure of the leg on the table, and thus the stagnation and prevention of venous return become greater.

I would like to show four slides demonstrating the effect of the Pneumatic Circulator on the venous pressures in the calf of the leg of the patient on the operating table.

(Slide) These are catheters placed within the leg veins. The patient is in a horizontal position. A 15-degree Fowler position increases the pressure within the leg at this point. The patient is brought back to horizontal again, then placed in the Trendelenburg position at 10 and 20 degrees, then back to the horizontal. These are pressures within the popliteal vein without the use of the pump.

(Slide) The next slide shows what happens to the pressure as measured by the catheter within the lesser saphenous vein. The Pneumatic Circulator produces a systolic pressure of approximately 120 mg. Hg, down to 40 or 30 mg. Hg diastolic, then back up to 120 systolic. This simulates muscular activity and thus aids the return of blood throughout the operative procedure.

(Slide) This slide shows the same pressures within the greater saphenous vein; at this point the catheter became obstructed by a clot, and we obtained no further pressure readings until the catheter was irrigated. Then we obtained a tracing indicating the systolic and diastolic pressures within the popliteal vein. The same systolic and diastolic contractions are evident. These were obtained by introducing the catheter retrograde in the popliteal vein of the leg which was to be amputated. All vessels were cut and ligated except the popliteal vein and artery. Pressures were studied after the application of our Pneumatic Circulator. The increase and decrease with each pulsation are evident.

We feel that this enhances and supports the fundamental work that Dr. McLachlin has just demonstrated.

Just one point about Dr. Brush's paper. We have used our Pneumatic Circulator in treating postoperative lymphedema. We have had considerable difficulty in fashioning a gauntlet for the arm because of the different sizes and shapes of arms, and we are very much pleased to see the gauntlet that Dr. Brush uses. It is an excellent one, and I might suggest that he simply put that same gauntlet on the leg and use the pump as he uses it on the arm.

I have been a little derelict in the last year in continuing our work. Our paper on this subject was presented before the Association a year ago. I thought I would have some additional clinical material to report, but during the past year my machine mysteriously disappeared. I am quite certain a visitor picked up the machine in the hospital, since it was encased in a very nice engraved leather case. I am still waiting to see somebody on the streets of Omaha using the case as a shopping bag.

I have enjoyed both these papers, and I think they are fundamental studies of the pathological physiology in two conditions of historic interest.

DR. THOMAS C. MOORE, Indianapolis: It is a pleasure to have the opportunity of discussing this very interesting paper. I heartily agree with the statements by Dr. McLachlin concerning the role of muscle activity in promoting venous return. I think this is quite important. As to the effect of stasis, its presence and its relationship to the formation of deep venous thrombosis and the subsequent thromboembolism, I am somewhat less clear in my own thinking relative to the factors presented here.

I should like to discuss briefly the venous heart. Dr. Shumacker and I have been interested in this problem for several years, and have carried out numerous studies with venographic techniques, the majority of them being upon the dependent extremity. We have reached certain conclusions as to the physiology of venous return which I think have been quite helpful to us in elucidating the role of muscle activity in the so-called peripheral venous heart and venous return. We have found that an injection of radiopaque medium into the deep venous system in the groin is accompanied generally by a regurgitant flow downward. This is a constant feature and is absent only in diseased extremities. We found that with a radiopaque medium injected into the popliteal space, part of it goes downward against gravity, and a large segment passes cephaled against gravity in quiet dependency. We have also discovered that injection of the superficial venous system in the dependent extremity invariably in the presence of a competent deep venous system is accompanied by the proximal passage of radiopaque medium segmentally into the deep venous system and, against gravity, cephaled. The only time one encounters return of venous blood in the superficial venous system in the dependent extremity is when one meets deep venous obstruction.

Muscle activity is the major factor in promoting venous return against gravity from the dependent extremity, and this return is brought about almost exclusively by passage through the deep venous system. In recumbency, stasis in the lower extremity would appear to be a relatively insignificant factor. The complex factors, local and systemic, leading to intravascular venous

thrombosis and thromboembolism have remained obscure.

DR. ANGUS D. MCLACHLIN, London, Ont., Canada: We are now able to study venous return in the leg as a visible entity. A rapid cassette changer is not fast enough, and it is only with cineradiography that the detail in venous flow becomes apparent. The film can be mounted in a circle and then run continuously, studying first one part of the field and then another.

The "stream-line" appearance when blood containing dye of one concentration joins blood with dye of another concentration is very evident. This is akin to a river containing muddy water joining one that is clear. The streams run some distance before becoming homogeneous. In the pregnant rabbit, the "stream line" of the more oxygenated blood from the uterine veins stands out well against the dark blood in the thin-walled vena cava. I think you can see in the film the stagnant and more opaque blood in the soleus muscle being forced into a popliteal vein in which continued flow has produced dilution and a consequent less dense shadow.

Our ultimate goal is an attempt to maintain the soleus pump during the operative and postoperative periods. Physiologists have helped us in constructing an explosion-proof electrical system that will produce effective contractions of the calf muscles during anesthesia. Several small contractions close together are more effective than a single large contraction. We must standardize the method, and then only a prolonged clinical trial can determine whether the method will reduce the incidence of pulmonary embolism.

DR. JOHN A. MCLACHLIN, London, Ont., Canada: I would like to thank the discussants and say, in reply to Dr. Moore, that there must certainly be some stasis in the legs. If we place the leg horizontal and keep taking pictures up to five minutes, there will be little, if any, change in the dye. If we then move the leg, there is a marked decrease in the amount of the dye. I am sure a good bit of the blood must go back up through the deep circulation. We have filled the deep circulation by putting a tourniquet just above the ankle and injecting the superficial veins.

I would also like to point out that by using these pyelogram patients we have been able to study normal legs. The first two or three legs that we attempted to study had clinical evidence or need of phlebograms. Because they showed complete occlusion of the veins, we were unable to study the normal physiology.

Experimental and Clinical Utilization of a Prosthesis for Replacement of the Trachea

RODMAN E. TABER, M.D., and LUIS TOMATIS, M.D., Detroit

Successful resection of cervical tracheostenosis with primary repair was reported in 1884 by Colley.[1] Experimental resection and reconstruction of the trachea were also mentioned.

In 1940, or 56 years later, renewed interest in partial circumferential (window excision) tracheal replacement was initiated by the investigations of Taffel.[2] Shortly thereafter, experimental efforts were directed toward replacement of tubular tracheal defects.[3,4] A combination of developments was probably responsible for this interest. In addition to the increasing use of endotracheal anesthesia for intrathoracic procedures, there occurred a realization by some pathologists and surgeons that the group of primary tracheobronchial neoplasms variously termed carcinoid tumors, bronchial adenomas, or salivary gland tumors of the trachea were in fact slowly invasive, malignant neoplasms. The first reported successful tubular excision and prosthetic replacement of the human trachea was carried out in such an instance by Belsey[5] in 1945. The patient had been subjected to a window-type excision of a cylindroma of the lower trachea the previous year. Local recurrence necessitated reoperation. The intrathoracic trachea between the thoracic inlet and the carina was replaced with a steel spring covered with fascia lata. The patient succumbed to extension of the neoplasm one year later. Eight tubular resections of the trachea utilizing a variety of reconstructive methods were subsequently reported by Clagett[4] (1946), using a polyethylene tube; by Jarvis[6] (1947), using a stainless-steel tube; by Rob[7] (1948), using tantalum mesh and fascia; by Ravitch[8] (1951), using tantalum mesh covered with dermis, and by Cotton and Penido[9] (1951), utilizing a stainless-steel tube.

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From the Division of Thoracic Surgery of the Henry Ford Hospital.

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The indications for partial or total excision of the trachea are infrequently encountered and largely represented by a variety of primary tracheal neoplasms. In a series of 507 collected cases, Ellman and Whittaker[10] found 20 different types; however, the majority fell into two categories, carcinomas and cylindromas. Among 47 cases of malignant tumors of the trachea reported by Moersch, Clagett, and Ellis,[11] 40% were squamous-cell carcinomas, and cylindromas accounted for 38%.

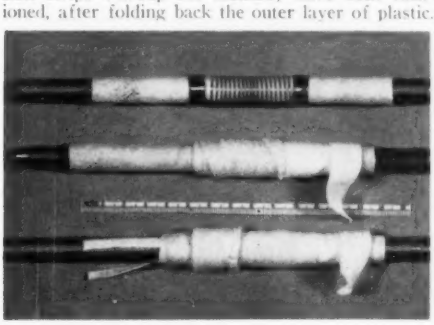
Reconstruction following partial circumferential excision of the trachea for small, localized neoplasms has readily been managed through use of the wire-reinforced dermis method of Gebauer[12] or of wire mesh covered with fascia.[13] Short tubular resections, three to five tracheal rings in length, have been successfully reconstructed by primary anastomosis.[14] Total or near-total excision of the trachea has been necessary in several of the previously reported cases, as well as the one to be described in this presentation. A satisfactory tracheal prosthesis will be required for the successful management of these patients.

Following the disappointing results obtained with experimental tracheal homografts,[15-17] investigation has largely concerned the metallic meshes and the nonporous, rigid metallic tubes. Because of the strength and resistance to kinking,

stainless-steel mesh is apparently superior to tantalum.[17] Autogenous dermis [8] or fascia [4,7] may be used to effect an airtight seal external to the metal support. Airway obstruction has been observed, due to progressive stenosis with this type of reconstruction [4]; however, several patients have maintained adequate airways for as long as one year. Rigid, nonporous metallic or plastic tubes, although satisfactorily positioned by the initial suture fixation, have uniformly lost this attachment later in the postoperative period. Airway obstruction due to movement of the free intraluminal tube, has been noted and necessitated reoperation for refixation of the prosthesis in at least one instance.[9] Progressive tracheal stenosis results if the rigid tubular support is removed.[6]

Two significant shortcomings, therefore, of the previously used tracheal substitutes are evident. These are the occurrence of stenosis at the tracheoprosthetic junction which follows tracheal retraction due to loss of prosthesis fixation, and the lack of incorporation of the prosthesis into host tissues. In an attempt to avoid these complications, we have constructed a tracheal substitute of compressed polyvinyl formalinized sponge (Ivalon) sponge which contains a stainless-steel coil for internal support. This relatively inert plastic was chosen in order that it might serve as a framework for infiltration by host tissues. This type of fibrous tissue substitution has been observed in connection with the use of polyvinyl sponge in atrial and ventricular septal defect closure and when it is used as a vascular conduit.[18,19] Stenosis at the site of the tracheoprosthetic junction is usually caused by disruption of this union, followed by progressive cicatricial contraction of the trachea. In the prosthesis under investigation, a small stainless-steel band at each end of the coil is secured within the tracheal lumen to prevent contraction of the divided tracheal ends.

Fig. 1.—Construction of the Ivalon sponge and stainless-steel spring tracheal prosthesis. The first step, in which the flexible spring is passed over the inner layer of compressed Ivalon sponge, is shown at the top. The outer layer of plastic sponge has been partially applied in the stage of fabrication shown in the middle of the photograph. Bias tape is used to separate the outer and inner layers in the area where the cuff is to be formed. A completed prosthesis is shown in the lower portion of the pictures. In this instance, the Ivalon tension strips (Group III method) have been fashioned, after folding back the outer layer of plastic.



Method and Materials

Thirty mongrel dogs, 10 to 14 kg. in weight, have been subjected to resection and replacement of varying lengths of the thoracic trachea. Under ether anesthesia, the trachea has been exposed through a right fourth interspace thoracotomy. The mediastinal pleura overlying the trachea has been developed as a flap for later use in covering the prosthesis. Ligation and division of the azygos and subclavian veins facilitate exposure of the trachea. A prosthesis of appropriate diameter and length is selected from an assortment of sizes (an internal diameter of 14 mm. is satisfactory for most animals of this size). The length of the prosthesis may be adjusted during fabrication by varying the length of the stainless-steel spring (Fig. 1). The prosthesis is constructed in a manner similar to that used for vascular substitutes, which utilizes the thermoplastic qualities of polyvinyl sponge.[19] Previously washed and thoroughly dried Ivalon sponge of surgical grade is cut into strips of 1.5 mm. thickness and 4 cm. width. Two layers are wound in a spiral manner on a mandrel and firmly compressed with a covering of roller bandage. This portion of the prosthesis is then autoclaved in a pan of water at 250 F and 20 lb. pressure for seven minutes. After removing the gauze covering, the metal spring is passed over the compressed sponge. The spring is soldered at each end to a stainless-steel band of 0.015 in. wall thickness and 3 mm. width. A two-layer covering of sponge strips is applied. In order to form a cuff at each end of the prosthesis, the inner and outer layers of plastic are prevented from fusing together in these areas by interposing a strip of bias tape 1.5 cm. wide between them. Compression

of the plastic sponge is again obtained with bandage and the heat-setting treatment repeated to complete fabrication of the prosthesis. Three to eight tracheal rings have usually been excised. Reconstruction is carried out with a prosthesis slightly longer than the defect to reduce suture-line tension. After division of the trachea at the distal site of resection, a sterile, flanged endotracheal tube is inserted by the operator into the distal trachea or one of the main-stem bronchi. The proximal end of the endotracheal tube is passed from the operative field to the anesthetist and ventilation resumed. An umbilical tape sling is tightened about the distal trachea to effect an airtight seal. The trachea is divided proximally and prosthesis fixation carried out first at this site. Three types of fixation have been investigated. In Group I (nine animals) the end of the prosthesis is placed within the tracheal lumen and the divided end of the trachea sutured to the base of the plastic cuff, which has been folded back upon itself. These sutures, three or four in number, approximate and seal the junction of the trachea and prosthesis (Fig. 2). The cuff is now unfolded and drawn over this suture line, where it is tacked to the trachea. Group II (10 animals) tracheal substitutions have been made by supplementing the suture line used in Group I with four tension-relieving sutures of 000 silk, which are passed around the third cartilage beyond the resection site. These sutures are also passed through the prosthesis and include the steel band at the end. These are placed before the other suture line and used to draw the prosthesis into the trachea. Later they are carried through the unfolded cuff and tied externally (Fig. 2). In Group III (11 animals) the same suture line was made as in Group I following application of two tension sutures of compressed Ivalon sponge. These 3-mm.-wide strips of plastic arise at the ends of the prosthesis, from which point within the tracheal lumen they are passed through small incisions in the wall between the third and fourth cartilages beyond the site of tracheal division. These suspender-like strips are then sutured to the outer, or cuff, layer of the plastic (Fig. 3). Following completion of the proximal anastomosis, the endotracheal tube placed by the operator in the distal trachea is removed and the original tube, which had been withdrawn into the cervical trachea, is passed through the prosthesis and into the lower trachea. Fixation is then carried out distally in a manner similar to that previously described. The umbilical tape sling is intermittently loosened to allow passage of sutures out of the tracheal lumen. The mediastinal pleura is closed over the prosthesis after suturing any residual needle-hole air leaks in the plastic. The thorax is closed without drainage after expansion of the lung. Antibiotics have been administered for five days postoperatively. Chest roentgenograms have been taken on the second and seventh postoperative days.

Results

All of the 30 dogs undergoing replacement of various lengths of the thoracic

Fig. 2.—Diagrammatic representation of prosthesis fixation method used in Group II replacements. (*a*) The tension sutures are passed around the third cartilage. (*b*) Sutures between the trachea and the base of the rolled-back cuff effect an airtight union. This row of sutures was the sole method of fixation used in Group I. (*c*) The tension sutures are passed through the unfolded cuff and tied. (*d*) Cross section of completed anastomosis.

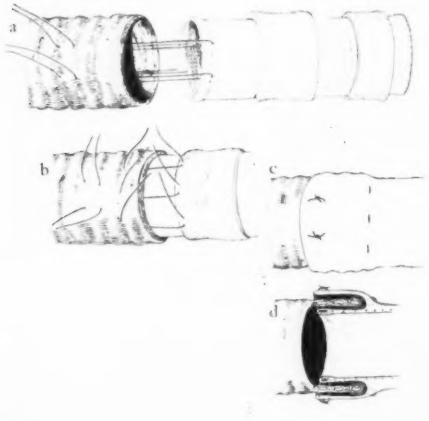
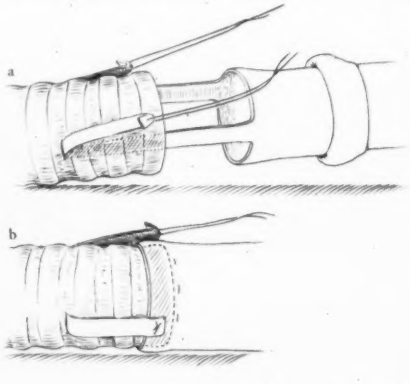


Fig. 3.—Method of fixation used in Group III experiments. (*a*) By the use of traction sutures, the Ivalon strips have been passed through the trachea. (*b*) The end of the prosthesis is pulled into the trachea. Sutures are then placed between the trachea and the base of the cuff, which is folded back, as in the previous two methods of fixation (shown as already tied). For clarity, the sutures used to secure the cuff to the trachea are not shown.



trachea have survived the operative procedure for at least seven days. With one exception, all have lived one month or longer. Evaluation of the prosthesis position and patency of the airway has been made with chest roentgenograms and repeated bronchoscopic examinations. Retraction of the trachea from the radiopaque prosthesis has been demonstrated in the roentgenograms by marking the tracheal position with a silver clip. By this means, separation of these two points is readily observed. It has been possible by these methods to detect early tracheal retraction and therefore predict the development of progressive tracheostenosis by the end of the first postoperative week.

In Group I (nine animals) there was a single suture line made at the base of the prosthesis cuff. These sutures frequently caused necrosis of cartilage, resulting in partial or complete disruption of the union. Slowly progressive airway narrowing has been noted in most of these animals. Six dogs in this group have died or been killed at intervals of between 4 and 10 weeks postoperatively because of progressive tracheostenosis. Two of these dogs developed perforation of the adjacent esophagus due to erosion by the displaced end of the prosthesis. The remaining three have maintained satisfactory airways during periods up to six months.

In Group II (10 animals) the prosthesis fixation was modified by the use of tension-relieving sutures which were passed through both layers of the plastic sponge and the trachea. Six animals in this group have died or been killed as a result of airway difficulties. One died at seven days, of pneumothorax, and five at 2- to 11-week intervals postoperatively, as a result of tracheostenosis. The modification of suturing used in this group did not improve upon the results obtained in Group I. The additional tension sutures were ineffective in preventing necrosis at the suture line, which was followed by tracheal retraction and narrowing due to scar formation.

Group III (11 animals) tracheal substitutions were performed with a minimum of sutures. Three or four have been placed at the base of the cuff, as in Group I, to maintain an initial air seal. A different type of tension-relieving suture was used, consisting of two narrow strips of Ivalon sponge. Because of the comparatively broad surface and elasticity of these bands, there has been no tendency to pressure necrosis of cartilage rings. Tracheal retraction and prosthesis migration have not been observed in this group of experiments during two months of observation. All animals have maintained a satisfactory airway (Fig. 4). Although the time interval has been shorter than in Groups I and II, these findings would appear significant, inasmuch as tracheal retraction, when it occurs in these experiments, has been apparent within two weeks.

The Ivalon sponge prosthesis is rapidly encased in a neomembrane of organizing granulation tissue, which firmly unites the tracheal ends over the outer surface of the plastic. This granulation tissue becomes adherent to the plastic within two weeks. Microscopically, the porous Ivalon is rapidly infiltrated throughout with fibrous tissue (Fig. 5). As has been demonstrated by

Fig. 4.—Experimental tracheal replacement two months after insertion (Group III method). Fibrous tissue surrounds the prosthesis and unites the ends of the trachea over the surface of the plastic. The ends of the prosthesis remain within the tracheal lumen as originally positioned. Preparation of the specimen has produced some separation between the plastic and the surrounding fibrous tissue, which accounts for the apparent difference in tracheal and prosthesis diameters.

Fig. 5.—Photomicrograph of experimental tracheoprosthetic junction two months after operation. The light areas in the lower portion of the photograph represent the plastic sponge of the prosthesis. The plastic is covered on the outer aspect (lower edge of section) with a neomembrane of organizing granulation tissue, which is infiltrating the porous sponge. The tracheal cartilage is united to the plastic prosthesis by fibrous tissue.

Bing,[20] the Ivalon sponge can in time be expected to undergo slow dissolution and phagocytosis. A collagenous tube supported by the steel spring would result. A true epithelial lining in the prosthesis lumen has not as yet been observed. In spite of the absence of ciliated epithelium in this area, the animals have not exhibited difficulty in handling their own secretions. They would very likely be handicapped in the presence of increased secretions due to pneumonia or aspiration.

Presentation of Cases

A 37-year-old woman secretary was first seen at Henry Ford Hospital on May 16, 1957. She complained of low-back pain of two months' duration and cough with intermittent wheezing during the previous week. Positive physical findings consisted of inspiratory and expiratory wheezes throughout both lung fields and limitation of lumbar spine mobility. Radiologic examination of the lumbar spine failed to reveal abnormalities. Chest fluoroscopy demonstrated partial left lower lobe atelectasis, and a barium swallow showed an abnormal impression on the esophagus above the aortic arch (Fig. 6). A routine peripheral blood study showed a hemoglobin of 11.1 gm. % and a white blood cell count of 13,400 per cubic millimeter. Severe asthmatic symptoms prompted emergency admission the following day. At the time of bronchoscopy, on May 27, a mass of tumor tissue was removed from the carinal region, with immediate improvement in the respiratory distress.

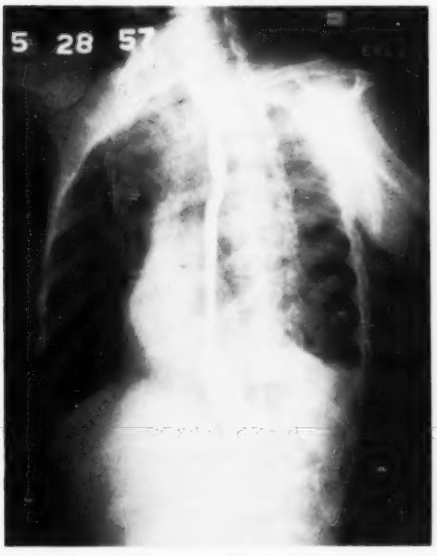


Fig. 6.—Preoperative chest roentgenograms of 37-year-old patient with reticulum-cell sarcoma of trachea. There is evidence of mass between the trachea and the esophagus above the aortic arch.

Fig. 7.—Postoperative chest roentgenogram following resection and replacement of thoracic trachea. The tracheostomy tube is visible at the upper end of the prosthesis.

The pathologic diagnosis was undifferentiated carcinoma of the trachea. Left thoracotomy and left main-stem bronchotomy were carried out on June 6. No gross abnormalities were noted. Frozen-section examination of a transbronchial biopsy specimen and a regional lymph node failed to reveal tumor tissue. The bronchotomy was closed and the operation terminated. Owing to increasing airway obstruction, bronchoscopy was repeated on June 19. A tracheal neoplasm was visualized extending from a point 3 cm. below the glottis to a level 1 cm. proximal to the carina. Thorough evaluation of the trachea was possible at the time of this elective bronchoscopy. It was then apparent that the tumor mass removed from the carinal area at the time of the original emergency bronchoscopic examination was tissue displaced ahead of the bronchoscope during the urgent attempt to improve the patient's airway. Emergency bronchoscopy was again required on June 27. The patient's respiratory status indicated that tracheal resection and replacement would have to be carried out at that time. Anesthesia was induced and initially maintained through the bronchoscope. Utilizing separate right fifth interspace thoracotomy and cervical incisions, the trachea between a point 1 cm. proximal to the carina and the first tracheal incartilage was resected and replaced with an Ivalon sponge and stainless-steel spring prosthesis, like the one under experimental investigation. The prosthesis measured 12 cm. in length, with an internal diameter of 17 mm. The intrathoracic anesthesia management was readily carried out, as described in the experimental procedure. Partial esophagectomy and end-to-end esophagoesophagostomy were necessitated by invasion of this structure with neoplasm. The esophageal anastomosis was made at the level of the thoracic inlet and the proximal tracheal reconstruction through the cervical incision. Tracheostomy completed this portion of the procedure, and the thoracotomy incision was closed with drainage. Progress chest roentgenograms demonstrated complete expansion of both lungs (Fig. 7). An unobstructed airway was present. Convalescence progressed satisfactorily, until the occurrence of massive hemoptysis on the 22d postoperative day, resulting in death of the patient. Necropsy demonstrated erosion of the innominate artery by the neoplasm. The prosthesis was somewhat larger in diameter than was ideally suited for this patient's trachea but had remained in place. Blood had entered the tracheobronchial tree through a defect in the distal anastamosis. Final pathologic diagnosis was reticulum-cell sarcoma of the trachea with secondary involvement of the esophagus, mediastinum, fourth lumbar vertebra, and right scapula.

Summary and Conclusions

Only infrequently will the surgeon be called upon to replace extensive tubular seg-

ments of the trachea. When the extent of the resection exceeds four to five tracheal rings in length, the need for prosthetic reconstruction arises. Previously reported tracheal substitutes which have received clinical trial consisted of nonporous metallic and plastic tubes or wire mesh covered with autogenous tissue, such as fascia or dermis. The postoperative problems involved with the use of most of these have usually occurred late in this period. These difficulties were secondary to loss of prosthesis fixation, with resulting tracheostenosis due to contraction of the tracheal ends or migration of the tubular foreign body within the tracheal lumen. It would appear that one solution of this complication is the use of a prosthesis fixation method which is ultimately dependent upon infiltration by host tissues, resulting in incorporation of the tracheal substitute into the remaining airway as a permanent structure.

A tracheal substitute consisting of a stainless-steel spring imbedded within Ivalon sponge plastic has been developed to fulfill this requirement. Histologic examination of the Ivalon sponge at intervals up to six months after experimental implantation as a tracheal replacement has demonstrated extensive ingrowth of fibrous tissue from the host. Three methods of suturing have been evaluated in 30 experimental replacements. Twenty-nine animals survived more than one month. Simple suture of the trachea to the prosthesis was performed in nine animals and found to be unsatisfactory. A second group of 11 tracheal substitutions was done, using additional sutures placed in a manner to relieve tension and prevent tracheal retraction. Progressive tracheostenosis occurred frequently in this group as well, indicating the unsatisfactory character of the fixation. A third group, of 10 experimental replacements, was carried out using tension-relieving sutures composed of narrow strips of Ivalon sponge. Airway complications, such as those observed in the previous two groups of experiments, have not been noted in this series during two months of observation. Tracheal retraction was prevented and the prosthesis incorporated into the airway structure.

Clinical utilization of this tracheal substitute has been made in the emergency management of a 37-year-old patient in whom it was necessary to replace the entire thoracic trachea which was involved by reticulum-cell sarcoma. A satisfactory airway resulted, until the patient died on the 22d postoperative day of hemorrhage due to erosion of the innominate artery by neoplasm.

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DISCUSSION

DR. KARL P. KLASSEN, Columbus, Ohio: I don't think Dr. Taber should be discouraged by this bleeding in his patient, terminating what we think is a very beautiful clinical experiment.

As you know, total replacement of the trachea is something we have all been considering. We have had difficulties with it. We have used various types of prostheses, stainless-steel tubes, and tantalum, Gebauer grafts, and so on. They all leave something to be desired in their application. We do need a good prosthesis, and this one appears to be quite good, because, as you know, Ivalon sponge will be impregnated by cells and will become fixed with tissues, and in that way it will serve very nicely as an airway.

When I saw the prosthesis, it looked quite good; and I think it can be made in every medical shop and should be available at all times. It is amazing that in Dr. Taber's case also erosion was the cause of the patient's death. We had a patient who went along for a year with a tantalum tube replacing the trachea, and this patient also died as a result of erosion of the innominate artery. Others have had difficulty also. I wonder whether these wire rings at the end could be modified by being made a little narrower so that they would not produce erosion.

It certainly appears to be an excellent device; and I don't think Dr. Taber should be discouraged, but should continue his work. As a matter of fact, I think we ought to have some of these prostheses in our operating rooms and use them in patients in whom we want at least short-term palliation, as well as in patients who have had extensive destruction of the trachea, where a long-term tube should be avaliable. I think Dr. Taber has made a very fine contribution.

DR. RODMAN E. TABER, Detroit: I want to express my appreciation to Dr. Klassen, who probably has had a good deal more experience in the clinical side of this matter than I have had.

(Slide) I thought it might be of interest to show this slide for the benefit of anyone who might be attempting this sort of thing experimentally. This method has proved to be very helpful in predicting results with this prosthesis. These silver sympathectomy clips are applied to the prosthesis and here to the ends of the trachea, the prosthesis being within the trachea from here to here. Displacement of the prosthesis is readily noted. These clips have been helpful.

Congenital Lesions of the Thorax in Infancy Demanding Early Surgical Treatment

RICHARD W. EGAN, M.D.; THEODORE C. JEWETT, M.D., and JOSEPH E. MACMANUS, M.D., Buffalo

Respiratory distress in the young infant is a common occurrence. Approximately one-half of the fatalities in the newborn are due to respiratory failure.[1] Among the congenital defects of the intrathoracic organs or supporting structures with surgical implications that present with respiratory distress are esophageal atresia with tracheal-esophageal fistula, mediastinal tumors and cysts, cystic disease of the lung, lobar emphysema, diaphragmatic hernia, patent ductus arteriosus, and pulmonary valvular stenosis. The presenting clinical pictures as seen at the bedside may be remarkably similar. The acute onset of dyspnea with varying degrees of cyanosis is common not only to these anatomical aberrations but to many medical and central nervous system lesions. It behooves the pediatrician and the surgeon to be constantly alert to the possibility of a surgically amenable lesion as the cause of progressive respiratory and circulatory failure. Early surgical correction of these defects is attended with a low mortality rate, and dramatic improvement is often observed immediately.[2] The purpose of this paper is to describe five dissimilar congenital defects of the thorax that presented as acute respiratory problems. In all instances little or no lasting relief of symptoms was observed with supportive therapy, making early surgery mandatory. The infants were all 5 months of age or younger at the onset of their symptoms.

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Department of Surgery of the University of Buffalo School of Medicine, and the Children's Hospital of Buffalo.

Report of Cases

CASE 1.—A white male infant, 12 days of age, was admitted to the Children's Hospital on Aug. 5, 1955. A birth history revealed that the child was delivered at term, with no complications or abnormalities noted. At the age of 7 days, the mother noted that the baby's respirations were more rapid and that he became cyanotic when he cried. The infant was admitted to a hospital in a neighboring community and placed in an oxygen tent. The dyspnea and cyanosis became progressively more pronounced, and he was transferred to another hospital on his third day of illness. X-ray examination of the chest revealed a large cyst of the right lung. This was "needled," with some improvement, but he remained dyspneic and cyanotic out of oxygen. On the day of transfer to the Children's Hospital, an # 18-gauge needle was placed in the cyst and connected to an underwater seal drainage apparatus.

Physical examination revealed an acutely ill, cyanotic infant in marked respiratory distress. The rectal temperature was 99 degrees F; the pulse rate was 112 per minute, and the respiratory rate was 50 per minute. The right anterior chest was hyperresonant on percussion; breath sounds were absent, and fine rales were audible in the right apex. Normal breath sounds were heard over the left chest. The heart was shifted to the left and had a regular sinus rhythm with no murmurs. Urinalysis revealed a pH of 4.5, a specific gravity of 1.010, and 3+ albumin. The hemogram revealed a hemoglobin of 17.2 gm. %, a red blood cell count of 5,780,000, a white blood cell count of 14,200, and a differential cell count of 45% filament forms, 9% band forms, 42% lymphocytes, 4% eosinophils, and 2% monocytes. X-ray examination of the chest showed a large cystic area occupying the lower three-fourths of the right chest and measuring 7×5×7 cm. The cyst was filled three-fourths with air and one-fourth with fluid. This structure markedly displaced the mediastinum to the left, the heart being against the left lateral chest wall. There was considerable atelectasis of

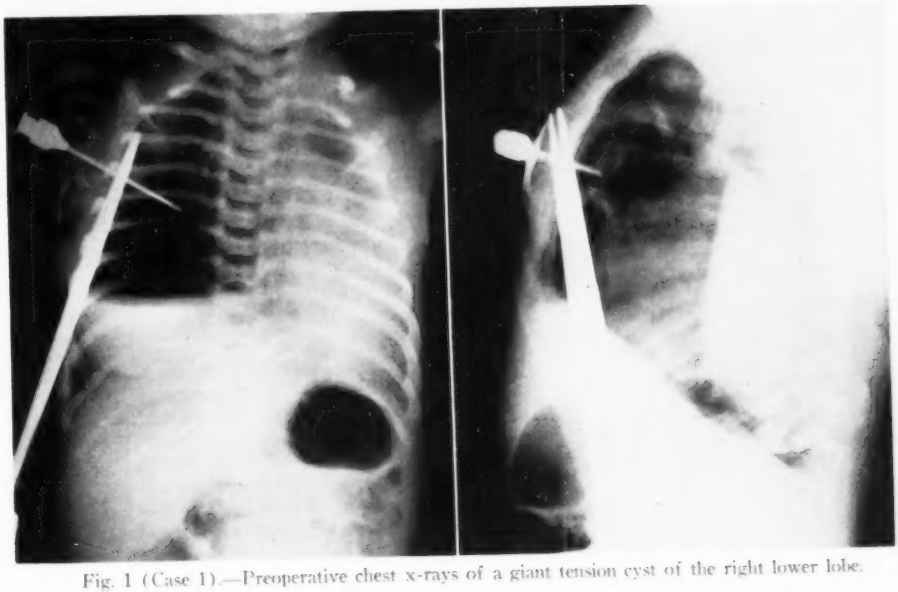


Fig. 1 (Case 1).—Preoperative chest x-rays of a giant tension cyst of the right lower lobe.

the left lung. A small amount of aerated lung was seen in the right apex and costophrenic angle (Fig. 1). The cyst was tapped with a 16-gauge needle, and 60 ml. of air under pressure was removed plus another 90 ml. of air, and 5 ml. of clean, straw-colored fluid was aspirated. The needle was fixed in place and connected to an underwater seal drainage system. The child was given antibiotics, oxygen, and parenteral fluids and was taken to surgery 20 hours after admission.

Operation (J. E. M.)

Under endotracheal, combined anesthesia the right chest was opened through the fourth intercostal space. The lower lobe was cystic and tense, compressing the upper lobe and shifting the mediastinal structures to the left. The cystic disease was confined to the basilar segments of the lower lobe. The superior segment was collapsed but not involved in the cystic disease. The middle and upper lobes appeared normal. The affected lobe was decompressed with a needle, and a left lower lobectomy was performed. The child had an uneventful postoperative course and was discharged on the seventh hospital day. Pathological examination of the specimen revealed a single large cyst of the lower lobe, measuring 5.5×3.5×4.5 cm. in the collapsed and fixed state. Histologically it was a typical bronchogenic cyst.

Follow-up examination of the child at one year of age revealed him to be asymptomatic, with normal growth and development. A chest x-ray showed the right upper and middle lobes to be completely expanded and the mediastinal structures in midline (Fig. 2).

Comment

Congenital cysts of the lung may be solitary, air- or fluid-filled, and involving a single segment or lobe, or they may be multiple, involving all or part of one or both lungs. The presenting symptom is dyspnea with or without cyanosis. The severity and progression of the symptoms are dependent on the extent of the disease, the size of the cyst, and the presence of a bronchial communication, resulting in a tension cyst. Physical examination will reveal a diminution in expansion of the chest on the involved side and absence of breath sounds in the area involved. Hyperresonance or flatness may be present, depending on whether the cyst is fluid- or air-filled. A translucent area with loss of lung and vascular markings will be noted on the chest x-ray. A large, air-filled cyst will give the appearance of a pneumothorax and may show herniation to the ipsilateral hemithorax, with marked shift of the mediastinal structures to the opposite side. Occasionally a fluid level may be seen within the cyst.

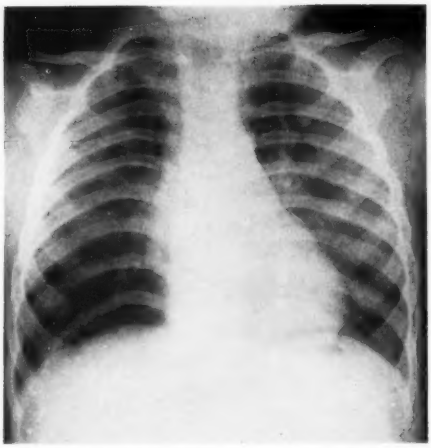


Fig. 2 (Case 1).—A chest x-ray one year following a right lower lobectomy for a giant tension cyst.

The urgency of the surgery is directly proportional to the degree of respiratory and circulatory embarrassment exhibited by the patient. A rapidly expanding tension cyst may require needle aspiration or drainage to obtain relief of the progressing respiratory failure. The surgical procedure of choice is a resection of the involved pulmonary division with the preservation of as much functioning lung tissue as possible.[3-6] This usually means a lobectomy. Since these lung cysts frequently become infected, their surgical removal should be accomplished at an early date.

Case 2.—A white male infant, 2½ months of age, was admitted to the Children's Hospital on Dec. 23, 1947. The birth history revealed that the delivery was difficult, the child showing multiple ecchymoses, and that the onset of spontaneous respiration was slow, necessitating mechanical resuscitative measures. The infant was delivered at term and weighed 7 lb. 6 oz. (3345 gm.). The baby was in apparent good health until the age of one month, when he developed some respiratory distress, with subcostal retraction on inspiration. At the age of 7 weeks he developed a cough, marked dyspnea, wheezing, and a fever. He was given chemotherapy and improved slightly. Twenty-four hours after admission his breathing became more rapid and labored.

Physical examination revealed an acutely ill infant in marked respiratory distress. The respirations were rapid and labored, and there were pronounced inspiratory and expiratory wheezes and substernal retraction. There was no cyanosis at rest, but he became "dusky" on crying. The rectal temperature was 99.6 F; the pulse rate was 138 per minute, and the respiratory rate was 36 per minute. The breath sounds were decreased throughout the entire left chest, increased in the lower right lung field, and diminished in the right upper lung field. Fine rales were heard at the right apex posteriorly. There were hyperresonance at the base and dullness at the apex of the right lung on percussion. The heart was shifted to the right, had a regular sinus rhythm, and no murmurs were audible. The liver edge was palpated 2.5 cm. below the right costal margin. Urinalysis was within normal limits, and the hemogram revealed a hemoglobin of 13 gm. % and a white blood cell count of 6550, with a differential cell count of 45% filament forms, 8% band forms, 42% lymphocytes, and 4% eosinophils. X-ray examination of the chest revealed an extreme degree of emphysema of the left upper lobe, a marked shift of the mediastinal structures to the right, and some atelectasis of the right upper lobe (Fig. 3). Bronchoscopy on Dec. 26 revealed no abnormality of the trachea or main-stem bronchi, although the orifice of the left upper lobe bronchus could not be seen because there was a slight bulge in this area. It was felt that this could be compatible with an overdistended left upper lobe. A culture of thin mucoid material grew out Escherichia coli. There was clinical and x-ray evidence of increasing distention of the left upper lobe with herniation of the lobe into the right hemithorax.

Operation (L. J. L.)

When the infant was 14 weeks of age, under endotracheal combined anesthesia, the left chest was opened through the fifth intercostal space. The left upper lobe was distended, tense, and bulged into the wound. The lower lobe was collapsed but expandable. A left upper lobectomy was performed, and the lobe did not deflate after extirpation. The child had an uneventful postoperative course and was discharged on the 14th postoperative day.

Pathological examination of the specimen showed a distinct acute diffuse alveolar emphysema of the left upper lobe.

The child has been asymptomatic since surgery, and when he was seen at the age of 3½ years, growth and development were normal. A chest x-ray revealed the left lower lobe to be reexpanded, with only a slight residual pleural haze over the upper third of the left lung (Fig. 4).

Comment

The exact pathogenesis of lobar emphysema is not known, although it does occur in the presence of pulmonary infection or

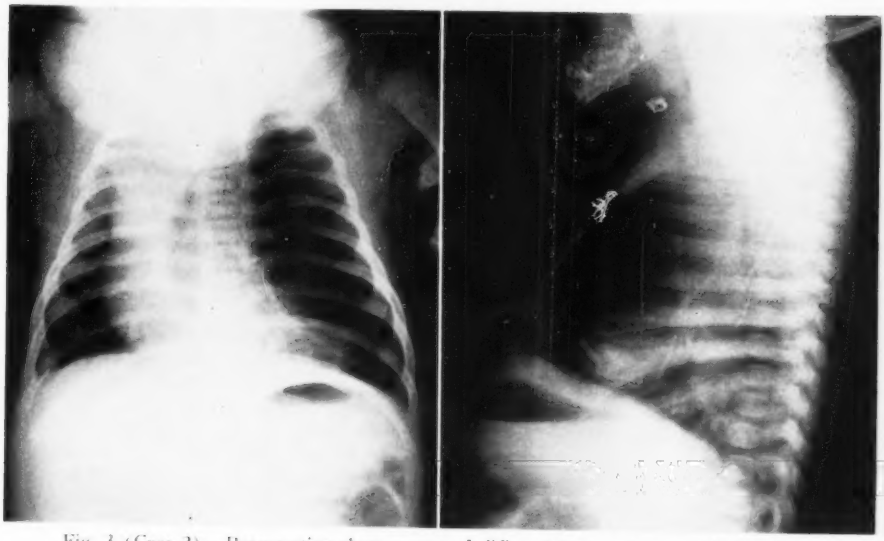


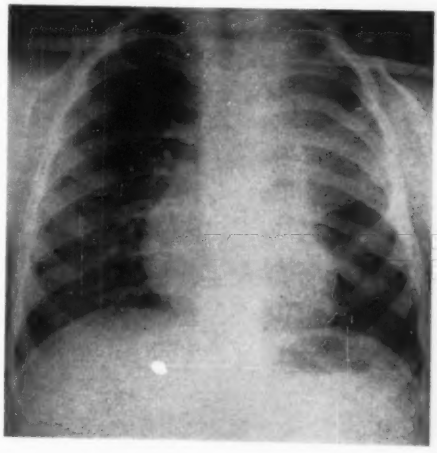
Fig. 3 (Case 2).—Preoperative chest x-rays of diffuse lobar emphysema of the left upper lobe with a mediastinal herniation of the overdistended lobe.

intrabronchial foreign bodies.[7-12] Other possible etiological factors that have been adduced to explain the obstructive emphysema are a deficiency or absence of the bronchial cartilaginous rings,[13,14] redundant bronchial mucosa,[15] and compression of the bronchus by a ductus arteriosus.[16] In many of the reported cases, no evidence of bronchial obstruction or abnormality could be found.[17,18]

The patients have respiratory difficulties early in infancy, manifested by dyspnea, cough, wheezing, and cyanosis. The onset is frequently mistaken for a pulmonary infection, but improvement does not occur with supportive and antimicrobial therapy. On examination the chest is hyperresonant on percussion, and the breath sounds are diminished on auscultation over the involved area. Frequently a respiratory wheeze will be noted. X-rays of the chest show extensive emphysema and compression of the adjacent lung tissue. The degree of mediastinal shift, presence of a mediastinal hernia, and atelectasis of the contralateral lung will depend on the extent and progression of the over distended lobe. In some instances the emphysema may be progressive.

Bronchoscopy should be performed prior to surgery to rule out the possibility of a nonopaque foreign body or other intrabronchial disease as the cause of bronchial obstruction. The profound, and often progressive, respiratory distress exhibited by these infants will make urgent surgery necessary. Immediately after removal of the involved pulmonary segment, marked symp-

Fig. 4 (Case 2).—A chest x-ray three years following a left upper lobectomy for lobar emphysema.



tomatic improvement occurs. Although all children successfully treated surgically have marked improvement, a number seem to be prone to respiratory infections and have wheezing respirations and dyspnea associated with these episodes.

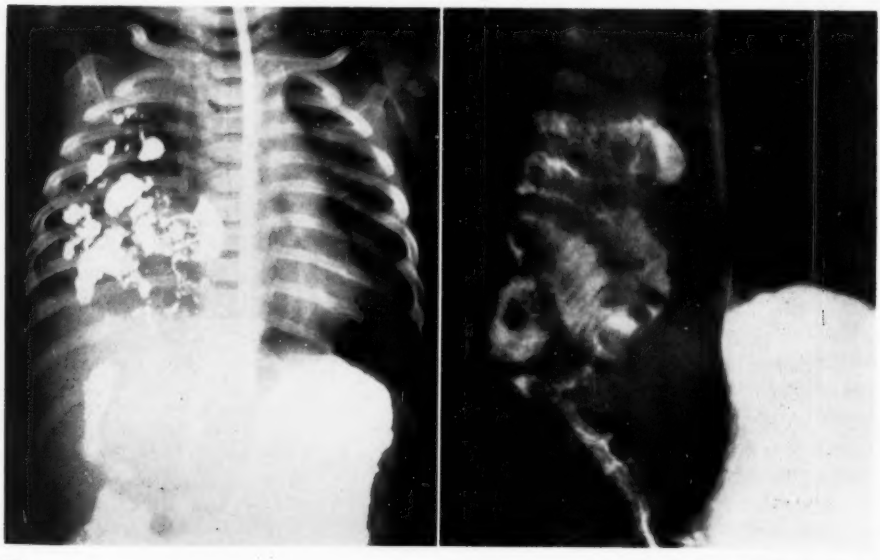
Case 3.—A white male infant, 5 months of age, was admitted to the Children's Hospital on Sept. 6, 1948. A birth history revealed that he was delivered at term with no complications and weighed 8 lb. 14 oz. (4026 gm.). The baby was in apparently good health and gaining weight adequately, weighing 18 lb. 6 oz. (8335 gm.), until nine days before admission. At this time the mother noted the onset of a dry cough, rapid, labored breathing, and vomiting. The infant was admitted to a hospital in a neighboring community with a diagnosis of pneumonia and treated with antibiotics and oxygen. The first chest x-ray was interpreted as showing a right lower lobe pneumonia. The symptoms continued unabated, and a second x-ray examination with a barium meal revealed a right diaphragmatic hernia. The child was transferred to the Children's Hospital 24 hours later.

Physical examination revealed an acutely ill, dehydrated infant in marked respiratory distress. The rectal temperature was 105 F; the pulse rate was 120 per minute, and the respiratory rate was 46 per minute. Marked sternal retraction was apparent on inspiration. The left chest was normal on examination. The right chest was dull to percussion over the right lung field posteriorly, and the breath sounds were diminished. No peristalsis or rales were noted. The heart was not enlarged, had a regular sinus ryhthm, and no murmurs were audible. The abdomen was not remarkable except that the liver edge was palpable 2.5 cm. below the right costal margin. The urine had a pH of 5.0, a specific gravity of 1.020, and no albumin or sugar. The hemogram revealed a hemoglobin of 14.4 gm. %; the red blood cell count was 4,820,000; the white blood cell count was 14,300, and the differential cell count was 49% filament forms, 9% band forms, 40% lymphocytes, and 2% monocytes. An admission chest x-ray revealed a homogeneous density over the base of the right lung. The right diaphragm could not be clearly visualized, and several flecks of barium were noted as high as the right third rib anteriorly. The child was hydrated, and a nasogastric tube was passed for decompression. A barium study was performed through the nasogastric tube; the stomach was seen to be markedly dilated, and multiple small-bowel loops were observed to have herniated into the right chest through the posterior aspect of the right hemidiaphragm (Fig. 5).

Operation (J. E. M.)

On Sept. 7, under endotracheal combined anesthesia, the abdomen was opened through a right rectus incision. The entire small bowel, the duodenum, most of the colon, and a portion of the right lobe of the liver were lying in the right chest. The herniation had occurred through a defect in the right pleuroperitoneal canal. The

Fig. 5 (Case 3).—A barium study of intrathoracic herniation of abdominal viscera through a defect in the posterior aspect of the right hemidiaphragm.



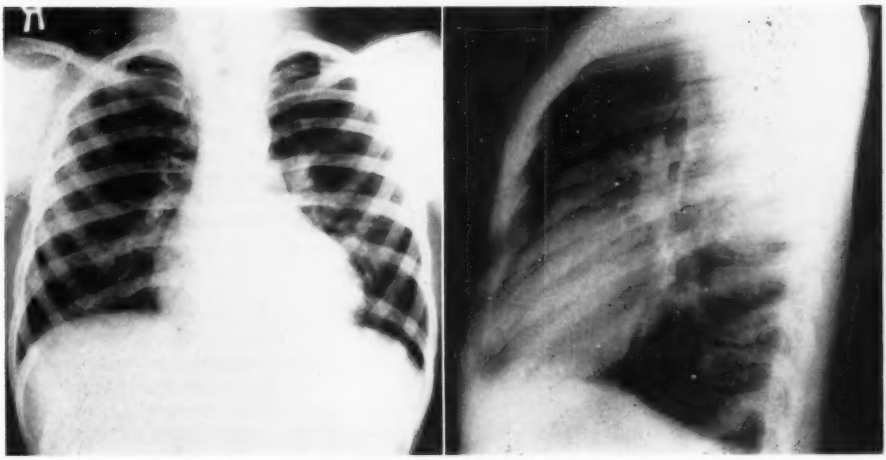


Fig. 6 (Case 3).—Chest x-rays six years following repair of a congenital diaphragmatic hernia through a defect in the right pleuroperitoneal canal.

defect in the diaphragm measured approximately 11×6 cm. The viscera were reduced into the abdominal cavity and the defect repaired with interrupted silk sutures. The postoperative course was complicated by a jejunojejunal intussusception, requiring surgical intervention on the 11th postoperative day. The child improved rapidly and was discharged on the 20th hospital day, weighing 15 lb. 14 oz. (7201 gm.). Examination six years later revealed that his growth had been normal; he was asymptomatic, and there was no clinical or x-ray evidence of any abnormality of the right chest, diaphragm, or gastrointestinal tract (Fig. 6).

Comment

A diaphragmatic hernia is a relatively common congenital defect in the newborn. Bowers, McElin, and Dorsey[19] reported 13 instances of a diaphragmatic defect in 15,556 deliveries. The mortality rate in this series was 92.3%. Only four of the infants had been submitted to surgery. The surgical literature is replete with reports of successful repair of congenital diaphragmatic herniae in infancy and indicates that early surgical intervention, especially in the newborn, is mandatory for survival.[20-23] The presenting symptom is marked respiratory distress, often accompanied by cyanosis. Occasionally vomiting will be noted. The excursion of the hemithorax containing the abdominal viscera will be diminished, as will the breath sounds. Percussion of the involved side will usually be tympanitic, and the cardiac dullness will be shifted toward the opposite hemithorax. Occasionally one may hear peristaltic sounds in the thorax. Anterior, posterior and lateral x-rays of the chest will usually confirm the diagnosis, the appearance of gas-filled intestinal loops being diagnostic. A study of the gastrointestinal tract by a barium meal is rarely necessary, and should be avoided. The hazards associated with barium meal may be minimized by employment of a nasogastric decompression tube for instillation of the contrast medium. Early surgical intervention is mandatory in infants with respiratory embarrassment from the herniation of abdominal viscera into the thorax. The transabdominal route for reduction of the hernia and repair of the diaphragmatic defect is preferred. The collapsed ipsilateral lung may not expand readily after the removal of the abdominal viscera from the thorax. In some instances the lung may show varying degrees of hypoplasia to account for this phenomenon.[24] Forceful attempts to reexpand the lung are to no avail and should be avoided. In a number of instances the collapsed lung will slowly expand.

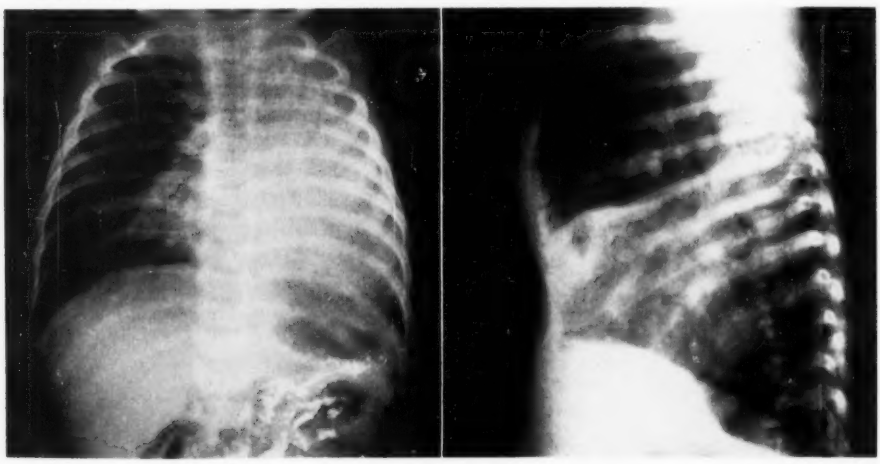
Case 4.—A white female infant, 3 months of age, was first admitted to the Children's Hospital on

June 4, 1956. A birth history revealed that she was delivered at term with no complications and weighed 6 lb. 9 oz. (2978). The child was well until the age of 2½ months, when she developed a dry cough. This became more persistent and was associated with dyspnea and cyanosis. The baby was admitted to a hospital in a neighboring community and treated with oxygen and digitalis. Two weeks following the onset of her illness she was transferred to the Children's Hospital for study.

Physical examination revealed a small, thin, pale infant with rapid, shallow respirations. Her admission weight was 7 lb. 13 oz. (3544 gm.); the rectal temperature was 97.8 F; the pulse rate was 152 per minute, and the respiratory rate was 52 per minute. There was a slight prominence of the left chest. The left chest was dull on percussion, and the breath sounds were diminished posteriorly. The heart was enlarged; a Grade 5, rough systolic murmur was heard in the third intercostal space along the left sternal border and was transmitted over the entire chest. The liver edge was palpated 1.5 cm. below the right costal margin. The urine was normal on examination, and the hemogram revealed a hemoglobin of 10.8 gm. %, a red blood cell count of 4,350,000, and a white blood cell count of 19,700, with a differential cell count of 68% filament forms, 14% band forms, 16% lymphocytes, 1% eosinophils, and 2% juveniles. An admission chest x-ray revealed a marked density over the entire left chest. The heart could not be accurately evaluated but appeared enlarged and shifted to the left. The trachea was in the midline, and the right pulmonary field appeared normal. An electrocardiogram was interpreted as showing a right bundle-branch block and combined ventricular hypertrophy. Therapy consisted of oxygen with aerosol, digoxin, and chloramphenicol. The infant slowly improved over the next 10 days. There was slight, progressive clearing of the left lower lung field, and she was discharged on a maintenance dose of digoxin. The baby was readmitted on July 1, 1956, at the age of 4 months with an exacerbation of her symptoms.

Physical examination revealed a poorly nourished and poorly developed female infant in acute respiratory distress. The rectal temperature was 103 F; the pulse was 180 per minute, and the respiratory rate was 84 per minute. The baby weighed 7 lb. 13 oz. (3544 gm.). The lips and nail beds were cyanotic. Sternal retraction was noted on inspiration, and scattered musical rales were heard in both lung fields. The heart was enlarged and a harsh, Grade 4, systolic-diastolic murmur was heard over the entire precordium, and a continuous thrill was palpable. The liver edge was felt 3.5 cm. below the right costal margin. Urinalysis revealed a pH of 5.0, a specific gravity of 1.024, a trace of albumin and sugar, 15-20 white blood cells, 4-6 red blood cells, and several granular casts per high-power field in the spun sediment. The hemogram revealed a hemoglobin of 9.9 gm. % and a white blood cell count of 10,550, with a differential cell count of 21% filament forms, 19% band forms, 56% lymphocytes, and 4% monocytes. X-ray examination of the chest showed more density over the left chest, with the left border of the heart completely obliterated (Fig. 7). There was a pneumonic process along the right border of the heart. Therapy consisted of oxygen with aerosol, digoxin, penicillin, chloramphenicol, and transfusions of packed red cells. A left thoracentesis

Fig. 7 (Case 4).—Preoperative chest x-rays of a patient with a large patent ductus arteriosus.



on two occasions failed to reveal fluid in the pleural space. The child improved slowly, and became afebrile and less dyspneic and cyanotic. On July 16 bronchoscopy was performed and no abnormalities were noted. A culture of the secretions of the left main bronchus grew out hemolytic Staphylococcus aureus, coagulase positive. A repeat bronchoscopy on July 21 showed only a decrease in the amount of secretions. The child remained afebrile and was gaining weight but still had a persistent tachycardia and dyspnea. The liver remained enlarged 3-4 cm. below the right costal margin, and serial x-rays of the chest showed clearing of the pneumonic process but no change in the density over the left lung.

On July 24, a cardiac catheterization was performed by Dr. Edward Lambert and a large left-to-right shunt, 2 to 4 vol. %, was observed at the level of the pulmonary artery. The pressures in the right ventrical and the pulmonary artery were moderately elevated but well under the femoral-artery systolic pressure. These findings were indicative of a patent ductus arteriosus with moderate pulmonary hypertension and a large left-to-right shunt.

Operation (R. W. E.)

On July 27, under endotracheal combined anesthesia, a left thoracotomy was performed and the chest entered through the fourth intercostal space. The left lung was almost completely collapsed, due to the tremendous enlargement of the heart. When the lung was freed, it expanded readily, and no abnormalities were noted. A continuous thrill was palpable in the region of the ductus arteriosus, extending along the pulmonary artery and well into the hilus of the left lung. The ductus was isolated and measured approximately 8 mm. in diameter, approaching the diameter of the descending thoracic aorta. The ductus arteriosus was temporarily obliterated, and no abnormalities of cardiac rhythm occurred. The ductus was then obliterated by multiple ligation at the junction of the ductus and aorta and at the pulmonary artery, with 0 silk. Two suture ligatures of No. 2 Atraumatic silk were then passed through the central portion of the ductus and ligated. The continuous thrill disappeared, although a moderate systolic thrill persisted in the pulmonary artery. The baby improved rapidly after surgery and was discharged on the 18th postoperative day, weighing 10 lb. 6 oz. (4706 gm.). Examination 11 months after surgery revealed the child to be asymptomatic, weighing 18 lb. (8165 gm.) and with no cardiac murmurs audible. A chest x-ray revealed the lungs to be clear and the heart of normal size and contour (Fig. 8).

Fig. 8 (Case 4).—Chest x-ray six months following surgical obliteration of a large patent ductus arteriosus.

Comment

The diagnosis of a patent ductus arteriosus usually does not present a problem. There is a significant percentage of cases of patent ductus arteriosus that do not present the typical findings and in which a diagnosis is extremely difficult. Many of the patients in this group are infants who fail to grow and develop normally, have repeated episodes of respiratory infections, and exhibit cardiac failure early. The presenting symptoms are marked respiratory distress, occasional cyanosis, particularly on crying, and evidence of cardiac failure. The heart is usually enlarged, and a loud, harsh systolic murmur is heard along the left sternal border. A palpable precordial thrill is frequently present. A widening of the pulse pressure is often noted. A chest x-ray examination will show cardiac enlargement, increase in the vascular markings, and an enlarged pulmonary-artery shadow. One should suspect the presence of a large patent ductus arteriosus in these instances, but other anomalies, involving left-to-right shunts, such as a high intraventricular septal defect or an aortic septal defect, can give similar findings.[25] Cardiac catheterization or angiocardiography will often confirm the diagnosis and should usually be done if

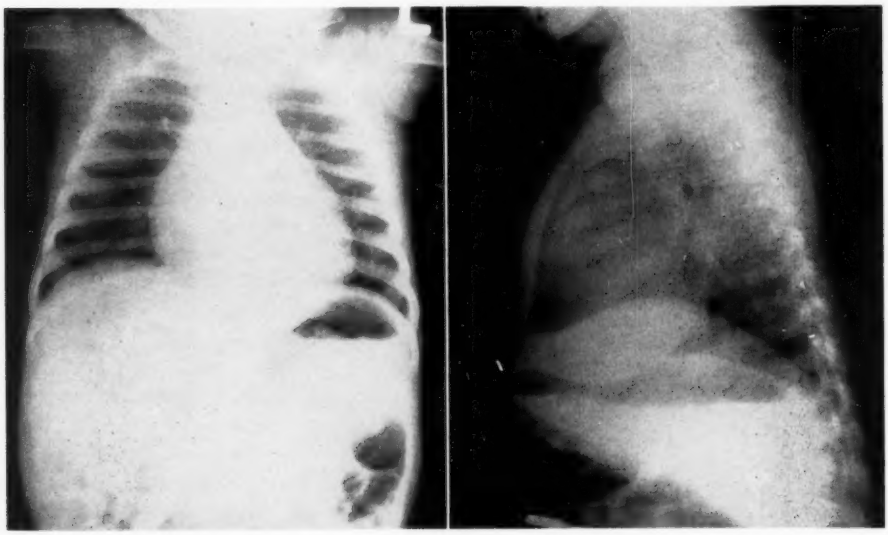
necessary in preference to an exploratory thoracotomy. Cardiac catheterization of patients with a large ductus arteriosus reveals a right ventricular and/or pulmonary artery hypertension and a large left-to-right shunt at the pulmonary level. In cases with a large ductus, passage of the catheter through the ductus to the aorta is not infrequent. The progressive cardiac failure or resistance of the cardiac failure to medical control will make early surgery for obliteration of the ductus arteriosus necessary. The mortality of surgical obliteration of a patent ductus in infants is low, and the beneficial results are immediate and lasting.[26]

CASE 5.—A white female infant, 4 months of age, was admitted to the Children's Hospital Nov. 10, 1955. The birth history revealed that she was delivered at term, with no complications or abnormalities noted, and weighed 7 lb. 6 oz. (3345 gm.). The child was asymptomatic and gaining weight adequately until two days before admission. At that time it was noted by the mother that the child was restless, breathed heavily, and that the lips and nail beds were bluish even at rest. The infant was seen by her family doctor, who administered an oral antibiotic. Because of the persistence of the signs and symptoms, the family doctor recommended hospitalization on the second day of illness.

Physical examination revealed a well-nourished infant who was markedly cyanotic and in severe respiratory distress. The admission weight was 12 lb. 12 oz. (5783 gm.); the rectal temperature was 99 F; the pulse rate was 124 per minute, and the respiratory rate was 84 per minute. Examination of the chest revealed scattered high-pitched rales in both lung fields. The cardiac sounds were distant and regular, and no murmurs were audible. The liver edge was palpable 2.5 cm. below the right costal margin. The oropharynx was reddened and edematous. The urine had a pH of 5.0, a specific gravity of 1.028, and 10-15 white blood cells were observed per high-power field in the spun sediment. The hemogram revealed a hemoglobin of 15.7 gm. %, a red blood cell count of 5,890,000, a white blood cell count of 9700, and a differential cell count of 58% filament forms, 1% band forms, 40% lymphocytes, and 1% basophils. A nasopharyngeal culture revealed hemolytic Streptococcus, E. coli, and hemolytic S. aureus. A blood culture grew out paracolon bacilli and hemolytic S. aureus, coagulase positive. X-ray examination of the chest on Nov. 11 showed the lungs to be clear and translucent, with a suggestion of decreased vascularity in the pulmonary fields. No pulmonary disease was noted, and the diaphragms were normal. The heart was normal in contour, the transverse diameter of the heart measuring 7 cm. and the transverse diameter of the chest measuring 13 cm. (Fig. 9). An electrocardiogram was interpreted as showing a moderate right ventricular hypertrophy.

Initial therapy consisted of oxygen, penicillin,

Fig. 9 (Case 5).—Preoperative chest x-ray study of a patient with a tight pulmonary valvular stenosis.



chloramphenicol, Cedilanid (crystalline lanatoside C), digoxin, and morphine. During the following eight days the child remained cyanotic out of oxygen with periodic episodes of marked respiratory distress and a steady loss of body weight. A faint, transient systolic murmur became audible in the pulmonic area, and by Nov. 25 a Grade 2 basal systolic murmur was apparent in the second intercostal space to the left of the sternum. Serial x-rays of the chest revealed no change in the size or contour of the heart. The child improved slightly and began to gain weight, but the intermittent episodes of respiratory distress and cyanosis continued. The liver continued to be enlarged. On Dec. 9 the child became severely dyspneic and cyanotic, this condition being followed by a period of apnea, which responded readily to therapy.

Operation (J. E. M.)

On Dec. 10, under endotracheal ether and cyclopropane anesthesia, the thorax was opened through a transsternal incision in the third intercostal space. The heart was greatly enlarged and bulged into the wound. The right ventricle was markedly enlarged and cyanotic. The pulmonary artery was dilated and soft, and appeared to be narrowed in the region of the pulmonic ring. No thrill or abnormality was felt along the right ventricular outflow tract. A probe was passed transventricularly through the right ventricle, and the impression of a tight pulmonary valvular stenosis was confirmed. There was no evidence of an infundibular stenosis. The appropriate Brock valvulotome was selected and passed transventricularly through the stenotic pulmonary valve into the pulmonary artery. Hegar dilators of increasing size were then passed transventricularly through the pulmonary valve up to a diameter of 1.6 cm. At the completion of the procedure the right ventricle became pink, and the pulmonary artery was full and tense with a palpable, rough systolic thrill. The general condition of the child improved dramatically, and at the conclusion of the operative procedure the baby was awake, crying without cyanosis, and moving about. Postoperatively she improved steadily and was discharged without medication on Jan. 3, 1956.

Follow-up examinations through September, 1957, have shown steady improvement and normal growth of the child. She has been asymptomatic, with no episodes of cyanosis or respiratory distress. Serial electrocardiograms have shown evidence of decreasing right ventricular hypertrophy. The most recent chest x-ray revealed a slight decrease in the cardiac size.

Comment

Severe disabling pulmonary valvular stenosis with a normal aortic root may be responsible for acute respiratory distress with cyanosis in infancy. The uncomplicated mild or moderate pulmonary valvular stenosis with a normal aortic root is usually asymptomatic, with the later onset of exertional dyspnea. True cyanosis is not usually present unless there is a right-to-left shunt through a septal defect. Characteristically a loud, harsh systolic murmur and thrill are present in the pulmonic area. Marked cardiac enlargement is not the rule, although the right ventricle is hypertrophied. Evidence of right ventricular hypertrophy may be seen on the electrocardiogram. X-ray examination of the chest will often show increased radiolucency in the pulmonary fields and an enlarged pulmonary-artery shadow. In severe pulmonary valvular stenosis, with a failing lesser circulation, the characteristic murmur may be absent or only a faint murmur audible in the pulmonic area. If intensive medical therapy fails to control the cardiac failure and repeated episodes of marked respiratory distress and cyanosis ensue, early surgery is necessary to relieve the valvular obstruction to the right ventricular outflow tract. The results of valvulotomy in such instances are usually dramatic, marked improvement of the infant often being observed immediately after the opening of the valve.

Summary and Conclusions

The acute onset of marked respiratory distress, often accompanied by cyanosis, may be the presenting clinical picture in many lesions of the young infant. The marked similarity of symptomatology in five markedly dissimilar congenital defects of the thoracic organs or supporting structures is presented. The acute onset of respiratory distress that did not respond to supportive therapy was present in all instances. Detectable evidence of cyanosis was noted in all but Case 3 (diaphragmatic hernia). Early and adequate x-ray examination of the chest was diagnostic for Case 1, a giant tension cyst of the lung; for Case 2, lobar emphysema, and for Case 3, a diaphragmatic hernia. The progressive nature of the re-

spiratory and circulatory failure in these infants precludes all but essential diagnostic procedures during the course of the evaluation. In all five instances early surgery was mandatory. Following the surgical amelioration of the congenital defect, rapid, and often dramatic, improvement was noted.

When a surgeon is confronted with an infant in marked respiratory distress, he must be constantly on the alert for dangerous congenital anomalies of the intrathoracic organs and supporting structures that demand early corrective surgery.

Dr. Leon J. Leahy permitted the report of Case 2.

100 High St.

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DISCUSSION

DR. THOMAS C. MOORE, Indianapolis: I should like to limit my comments to the phase of this problem dealing with diaphragmatic hernia. Dr. Battersby, Dr. Roggenkamp, Dr. Campbell, and I have been interested in this problem at the Indiana University Medical Center for some time. Last year we published our experience with 16 patients in whom the posterolateral type of diaphragmatic

hernia was encountered in the early neonatal period. Thirteen of the sixteen patients were seen during the first 40 hours of life. We found, as have others, that there is a great deal of difficulty with pulmonary expansibility in these patients seen during the early hours of life. The difficulty is most marked on the side of the diaphragmatic hernia. The lung simply does not expand properly in the majority of these infants. However, we do feel that early operation is most desirable to provide an optimum climate for subsequent pulmonary expansion. Eight of our thirteen clinical cases survived.

From the published experience of obstetrical services, it would appear that the majority of infants born with the posterolateral type of diaphragmatic hernia die during the early minutes and hours of life. In this regard, the experience of Dr. Dorsey and his associates from the Evanston Hospital is most revealing. They found, in their series of 13 patients, that the diagnosis in 9 was made at the autopsy table. The nine had died during the first two hours of life. Only four cases were diagnosed clinically, and only one of them survived operation. Similar findings have been reported by Dr. Edith Potter from the Chicago Lying-In Hospital. It is desirable to have all obstetricians quite aware of this problem. It would also be desirable to have some means of carrying out prompt roentgen studies in all newborn infants who do not breathe spontaneously at birth or who exhibit significant cyanosis during the early minutes and hours of life.

Earlier diagnosis is most imperative if a larger number of infants are to be salvaged. Because of the difficulty with pulmonary expansion, the use of some type of respiratory support, such as the pump-oxygenator, might offer a means of supporting these infants during the operation, and perhaps even during the early hours of life.

The last comment I should like to make concerns a 52-year-old patient upon whom I operated recently. He had a congenital posterolateral, Bochdalek type of hernia. The left hemithorax was almost completely filled with abdominal viscera. The left lung was quite small, collapsed, and fibrotic, with an area of emphysematous blebs. This fibrotic pulmonary remnant could not be expanded after reduction and repair of the hernia. This experience suggests that if one does not remove pulmonary compression early, one has little opportunity in late cases of materially improving respiratory function by any sort of operative procedure.

DR. COLIN FERGUSON, Winnipeg, Man., Canada: This is a very interesting paper. A fairly large number of small infants are admitted to hospital with severe distress as a result of their congenital lesion. The problem essentially is to be able to recognize early those lesions which can be treated effectively by surgery, because these babies are the ones whose lives can be saved.

I should like to show three slides which illustrate lesions which we have encountered at the Winnipeg Children's Hospital, and which were not specifically mentioned in this paper.

(Slide) This is the chest x-ray film of a newborn infant who was admitted to hospital in acute respiratory distress. As you can see, on the left side there is very marked pneumothorax, which in this baby appeared to be spontaneous in origin, as there was no history of vigorous resuscitative efforts, nor was there any evidence of underlying lung pathology.

The second x-ray film was taken approximately six hours after the first, and shows the complete expansion of the left lung after a tube had been placed in the left pleural space. The child was discharged from hospital on the third day.

(Slide) Here is another problem which in our hands has been difficult to solve. This baby was admitted to hospital in heart failure, and the x-ray film revealed a markedly enlarged heart, with pulmonary vascular engorgement. Other than being able to make a diagnosis of a very large left-to-right shunt, we have found it difficult to determine the exact cardiac defect in these seriously ill infants. It has been our practice to perform retrograde aortography through the brachial artery, in the hope that we could demonstrate a patent ductus arteriosus. If we do find an open ductus, we immediately take the child to the operating room and close the patent ductus under the same anesthesia as used for the aortogram.

The slide shows a retrograde aortogram in which a large patent ductus was clearly visualized in one of these small infants.

(Slide) Coarctation of the aorta causing heart failure early in life is frequently a difficult problem in surgical management. While it is true that some of these infants will improve on medical treatment, and thus can be operated upon electively at an older age, many will not survive unless they are operated upon early in life. The diagnosis of coarctation in a small baby is sometimes very difficult to make, because femoral pulsations may be present and blood pressures in small infants are difficult to obtain. The slide shows a retrograde aortogram performed on one of these children, and I believe that you can easily see the coarctation of the aorta.

I wanted to bring out these few points, because, as has been emphasized, if these conditions are recognized early in life, before the situation goes on to an irreversible stage, many of these infants can be saved by successful surgical treatment.

DR. ROBERT P. HOHF, Evanston, Ill.: I don't wish to prolong this discussion by giving case reports, but I arise simply to report one unusual circumstance which we have seen.

A newborn child with a normal delivery at the Evanston Hospital developed acute respiratory distress in 24 hours caused by hydropneumothorax, which was treated by drainage through an intercostal tube. The patient's condition improved immediately. Several hours later the nurse called with a report that changed the diagnosis for us. She observed feedings coming out of the intercostal tube. We immediately did an esophagogram, which showed a perforation of the esophagus on the right side above the diaphragm. Thoracotomy revealed this to be a typical perforation, which was closed. The baby's postoperative course was uneventful. Now, 18 months later, he is developing normally.

The lesion in this case may not be exactly congenital, but at least it brings up the point of esophagitis or other peptic inflammatory processes during intrauterine life, before delivery. There was no history of vomiting in this case.

DR. RICHARD W. EGAN, Buffalo: I wish to thank the discussers for their comments. We certainly agree with Dr. Moore that an infant with a diaphragmatic hernia should have the defect corrected surgically as soon as the diagnosis has been made. The most important consideration is that one be constantly aware of the possibility of a surgically amenable congenital thoracic defect when confronted with an infant exhibiting respiratory distress. These congenital anomalies can be fatal, and sudden death can occur with little warning, even in those with congenital cardiac defects.

In many instances, actually in three of the five problems presented, the diagnosis was established by good routine chest x-ray examination. Awareness of these congenital anomalies presenting as acute problems of respiratory distress will lead to earlier diagnosis and definitive therapy.

Rupture of the Main Bronchi in Closed Chest Injury

A Reproduction of the Injury in the Experimental Animal; Discussion of the Possible Mechanisms Involved

JAMES R. LLOYD, M.D.; DAVID K. HEYDINGER, M.D.; KARL P. KLASSEN, M.D., and L. CHANDLER ROETTIG, M.D., Columbus, Ohio

Five patients with rupture of the bronchi in closed chest injury have been treated at the Ohio State University Medical Center since October, 1955. All five patients had been involved in automobile accidents, and the trauma in each case was the result of a steering wheel injury (Fig. 1).

Clinical Study

CASE 1.—A 19-year-old white youth sustained a tear of the right intermediate and middle-lobe bronchus. The lesion was repaired 18 hours after trauma by primary suture, resulting in an uneventful recovery.

CASE 2.—A 16-year-old white youth suffered a complete severance of the left main bronchus, which was successfully repaired by resection of the injured segment and end-to-end anastomosis 16 days after trauma.

CASE 3.—A 21-year-old white woman sustained a bilateral avulsion of the bronchi, with disruption of the carina. This lesion was successfully repaired by performing a left pneumonectomy, reconstruction of the distal portion of the trachea, and an end-to-end anastomosis of the trachea and the right main bronchus. Unfortunately, the patient developed irreversible ventricular fibrillation and died four hours after trauma.

CASE 4.—A 27-year-old white woman sustained a complete severance of the right main bronchus. The diagnosis was made 15 minutes after trauma and was repaired by primary anastomosis approximately two hours later, with complete return of function. Ten days later, bronchoscopy was performed, and the region of the original trauma was identified only by a slight localized reddening of the bronchial mucosa.

CASE 5.—A 15-year-old white girl incurred a tear of the left main bronchus. Primary suture

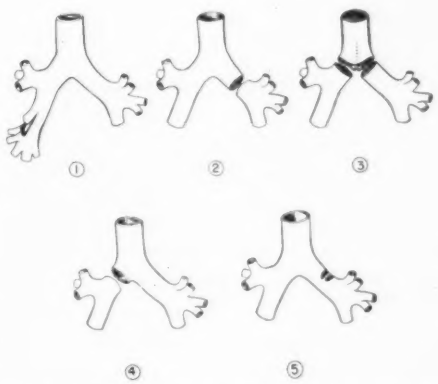

Fig. 1.—Four cases of rupture of the bronchus treated at the Ohio State University Medical Center and one case (*2*) treated at the White Cross Hospital, Columbus, Ohio.

Case 1: Laceration involving the right intermediate and the right middle-lobe bronchus in a 19-year-old youth.

Case *2*: Complete severance of the left main bronchus in a 16-year-old white youth.

Case 3: Bilateral avulsion of the bronchi and disruption of the carina in a 21-year-old white woman.

Case 4: Complete severance of the right main bronchus in a 27-year-old white woman.

Case 5: Laceration of the left main bronchus in a 16-year-old white girl.

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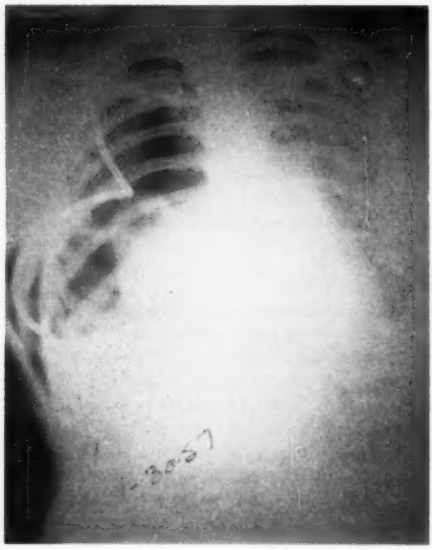


Fig. 2.—Portable chest film taken about 30 minutes after trauma. The patient (Fig. 1, *4*) had complete severance of the right main bronchus. Note the collapse of the right lung.

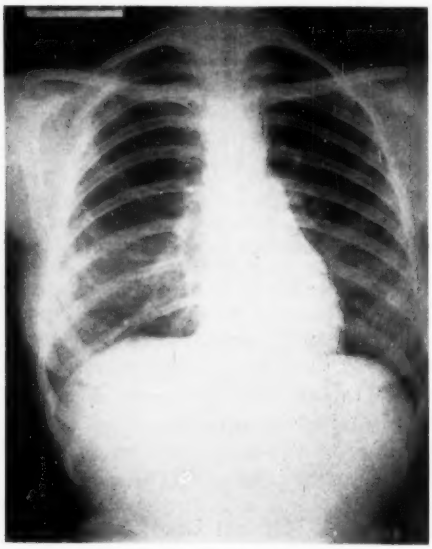


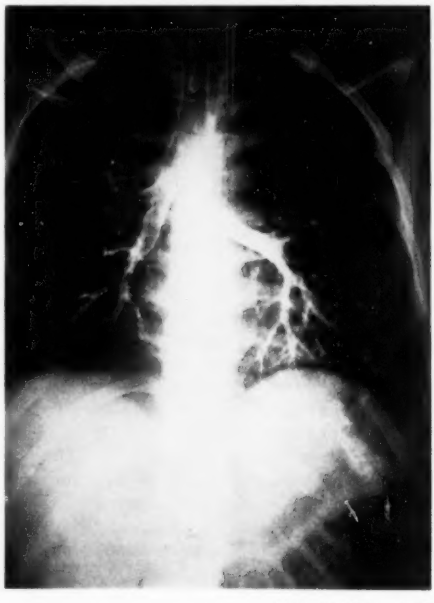
Fig. 3.—Posteroanterior chest film two and one-half months after trauma on the same patient as that in Figure 2, showing complete expansion of the right lung. Pulmonary function studies were within normal limits.

of the lesion was performed five days after injury, with an initial good result. An obstruction at the site of the repair developed, owing to granulations, and a bronchoplasty was necessitated three months later. This patient is still under observation, and a recent bronchoscopy demonstrated a partial occlusion, again at the site of injury, which is currently being managed by conservative means.

X-Ray Studies.—Figure 2 is a portable chest film of Patient 4. This was taken in the emergency room of the University Hospital and demonstrates persistent collapse of the right lung, in spite of high negative suction. Now, two and one-half months after primary anastomosis of the right bronchus, the lung is completely expanded (Fig. 3), and pulmonary function studies are within normal limits.

A bronchogram, performed on Patient 1 two and one-half months after primary repair, shows complete reexpansion of the lungs, without evidence of significant narrowing of the tracheobronchial tree (Fig. 4).

Fig. 4.—Bronchogram obtained about two and one-half months after primary repair of a laceration of the right intermediate bronchus and right middle-lobe bronchus. There is complete expansion of the right lung and no evidence of significant narrowing of the bronchus (Fig. 1, *1*).



Review of Literature

As a result of this clinical experience, we became interested in the lesion and collected 116 cases from the literature. Table 1 is a summary of these cases, based on survival and treatment. There were 20 early

TABLE 1.—*Summary of 116 Cases of Rupture of the Main Bronchi Collected from the Literature (1848-1956)*

I Early deaths	20
II Late deaths (1 hr.–96 hr.)	16
III Spontaneous recoveries	19
IV Surgical intervention	61

deaths (instantaneous, up to one hour), the majority of these patients dying before treatment could be instituted. Sixteen patients survived the initial trauma, living for 1 hour or more, up to 96 hours. There were 19 instances of spontaneous recovery, the diagnosis being made intra vitam by bronchography or bronchoscopy. Of these 19 patients, 5 died of causes other than the initial injury, and rupture of the bronchus was an incidental finding at the time of autopsy. Sixty-one of the patients survived the initial trauma and underwent various forms of surgical intervention, including pneumothorax, thoracoplasty, lobectomy or pneumonectomy, and various types of bronchoplastic repairs. Of these 61 patients, only 14 underwent surgical intervention during the first 24 hours.

Although the mode of production of the lesion was discussed at length in many of the studies, a satisfactory explanation of the mechanism of injury was not presented. We were unable to find any evidence that the problem was produced experimentally, except for one isolated instance. Iselen (1907) noted one instance of rupture of the bronchus while experimentally producing traumatic diaphragmatic hernia in rabbits, but made no attempt to explain the bronchial injury. To our knowledge, theories regarding the nature of the injury are primarily conjectural and hypothetical.

Some of the commoner hypotheses suggested in the literature are as follows:

1. Explosion of the bronchial tissue secondary to increased endotracheal pressure in the presence of a closed glottis at the time of the injury

2. Division of the bronchus by shearing forces, produced when the sternum is displaced against the vertebral column

3. Crushing of the bronchus between the posterior surface of the sternum and the vertebral column

4. A pulling apart of the bronchi due to lateral distraction of the lungs (This concept holds that as the thorax is compressed, the anteroposterior diameter of the chest decreases and the transverse diameter of the chest increases. The lungs are held in apposition to the chest wall by the intrapleural negative pressure and are obliged to move laterally with the chest wall, tearing the bronchi at the carina.)

5. Tearing of the bronchi resulting from the lungs being pushed apart by the sternum and mediastinal soft tissues, acting as a wedge insinuated between the lungs at the time of trauma

6. Lacerations of the bronchi by the sharp ends of fractured ribs

Experimental Study

Owing to the lack of experimental evidence explaining the mechanism of injury, the problem was taken to the Animal Laboratories, where the lesion was successfully reproduced under controlled conditions.

Methods.—Discarded or salvaged dogs were utilized for these traumatic experiments, and these were anesthetized with intravenous pentobarbital (Nembutal), after which they were intubated with a cuffed endotracheal tube. Two basic experimental conditions were established. In Series I the dogs were supine, and in Series II they were supported in the erect position. A heavy cloth bag was filled with sand and its weight adjusted to 50 lb. The mass, when dropped from 10 ft. and arrested within a distance of 4 in., after a free fall, exerts a force of 1500 lb. When it is dropped from 5 ft. the arresting force or retarding force is 750 lb.

In the Series I study, the weight was dropped, and in Series II the weight was swung pendulum fashion against the dog's chest. In order to ensure a uniform and reproducible blow, a standard piece of 2×4 in. lumber, 12 to 14 in. long, was placed flat against the dog's chest, midway between the suprasternal notch and the xiphoid process (Fig. 5).

After the blunt trauma had been inflicted, each animal was observed for a short while to determine whether or not signs of bronchial rupture could be detected. The ani-

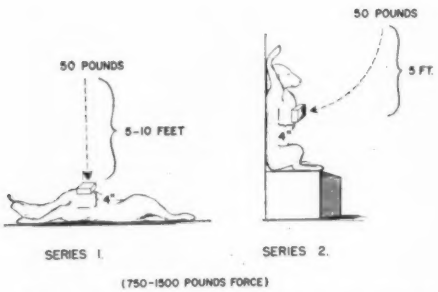


Fig. 5.—Position of the animals at the time of trauma. The block on the animal's chest was interposed between the point of impact and the impacting force to insure uniform trauma.

mals were then autopsied approximately 30 minutes after trauma and the nature and extent of injuries recorded.

Experimental Conditions and Considerations.—It has been generally proposed that the reflex closure of the glottis is one of the essential conditions for producing rupture of the bronchus from blunt chest trauma. The initial effort was directed toward determining whether or not this was a significant factor.

Thirteen dogs (Series I, Group 1) were subjected to blunt trauma, as described above, with an airway maintained open by a patent endotracheal tube. Rupture of a bronchus was seen to occur twice, an incidence of 15%.

Fifteen dogs (Series I, Group 2) were subjected to the trauma with a closed airway (cuffed endotracheal tube with the cuff inflated and the lungs in a state of inspiration). Rupture of the bronchus was observed in 10 instances, or 66% of the animals. In addition to rupture of the bronchus, a high incidence of fatal associated cardiac and vascular injuries was observed (Table 2).

TABLE 2.—*Summary of Experimental Results, Series I, Groups 1 and 2 (Supreme Position)*

No. of Dogs	Endotracheal Tube	Bronchial Rupture	
13	Open	2	(15%)
15	Closed	10	(66%)

Five dogs (Series I, Group 3) were traumatized with a closed airway, in addition to which blocks 3-in. wide were placed at either side of the dog's chest to arrest the blow just above the point where the anterior chest wall would be forced against the vertebral column. (The average anteroposterior thickness of the spinal column in a 25 to 30 lb. dog at the midthoracic level is about 2¾ in.) None of these dogs demonstrated rupture of the bronchi, nor were any fatal vascular injuries produced.

Six dogs (Series I, Group 4) were subjected to trauma with a closed airway, but the 3½ in. block of wood interposed between the chest wall and the source of trauma was changed to a block 6 in. wide, so that the blow would be distributed over a wider area of the anterior chest. Four of these dogs demonstrated minor mucosal tears of the bronchus, but in no case did the lesion involve the full thickness of the bronchial wall.

In order to determine whether or not position at the time of trauma influenced the type of lesion produced, the first two experiments in Series I were repeated in the upright position. The results indicated that there was no significant difference between the supine and the upright position.

Eight dogs (Series II, Group 1) were subjected to blunt chest trauma when in the upright position. The airway was maintained open by a patent endotracheal tube, and rupture of the bronchus was observed in one dog, or 12.5%.

In four dogs (Series II, Group 2) with a closed airway the bronchus was ruptured in each instance, or 100%.

A group of four dogs, not listed here because of the lack of controlled conditions, presented an interesting problem that led

TABLE 3.—*Summary of Experimental Results, Series II, Groups 1 and 2 (Upright Position)*

No. of Dogs	Endotracheal Tube	Bronchial Rupture	
8	Open	1	(12.5%)
4	Closed	4	(100%)

to an additional factor being introduced into the study. These dogs were being used to enlarge the number of cases in Series II, Group 2. The lungs were being hyperventilated to build up an excess of oxygen so that respiratory movements would not be made between the time the endotracheal tube was clamped and the trauma inflicted. Rupture of the bronchus did not occur under conditions in which at least a 60% to 70% incidence of rupture should have been observed. It was noted that while these dogs did not demonstrate any significant damage to the tracheobronchial tree or lung parenchyma, pneumothorax was present in all four cases. It was reasoned that the pneumothorax might have been present as a result of overvigorous pretrauma hyperventilation and that, if so, the presence of free air in the pleural cavity might act as a protection against the traumatic lesions that had thus far been produced. Therefore, it was decided to introduce measured quantities of air into the pleural cavities of a group of dogs to determine what effect pneumothorax might have.

Nine dogs (Series II, Group 3) were traumatized with closed airways when in the upright position. In the first dog of the series, with 25 cc. of air introduced into either side of the chest cavity, rupture of the bronchus occurred, as it did when 25 cc. was placed in the left side only.

Fifty cubic centimeters of air in each side of the chest of two dogs appeared to be a sufficient quantity to prevent rupture of the bronchus. An additional five dogs in this series were given 50 cc. of air in the left side of the chest only, and in none of the five dogs was rupture of the bronchus observed (Table 4).

TABLE 4.—*Summary of Experimental Results, Series II, Group 3 (Upright Position, Endotracheal Tube Closed)*

No. of Dogs	Pneumothorax	Bronchus Rupt.	Bronchus Intact
1	25 cc. bilat.	1	
1	25 cc. left	1	
2	50 cc. bilat.		2
5	50 cc. left		5

A right-sided pneumothorax of 50 cc. of air failed to prevent rupture of the bronchi in two out of five dogs. The reason for this discrepancy is not readily explained, except for the fact that the left main bronchus was ruptured in each case. This would indicate that the carina is fixed by the apposition of the anterior chest wall and the vertebral column, the left main bronchus being ruptured independent of the right side of the tracheobronchial tree.

An additional two dogs (Series II, Group 4) with the impact exerted against a block of wood 1½ in. wide and with a closed airway, did not incur rupture of the bronchus. Instead, massive tears and severe damage not previously observed were sustained by the lung parenchyma.

In an attempt to demonstrate the degree of chest deformity that results from this nature of trauma, two dogs were x-rayed while the chest was maintained in a state of maximal compression. The heart was shown to be displaced to the extreme left of the chest cage.

A total of 64 dogs were used in the overall study, and rupture of the bronchus was produced in 24 instances. Seventy-five per cent of the bronchial ruptures involved the left main bronchus. Thirty-nine dogs died as a direct result of trauma other than rupture of the bronchus. There were major tears of the superior and inferior venae cavae in four instances, and the liver was severely lacerated in six. There were 24 cardiac lesions, varying from minor auricular tears to complete avulsion of the left ventricle. Photographs (Figs. 6 and 7) demonstrate the nature of bronchial lesions produced by experimental closed chest trauma.

Comment

Extensive studies on blast injuries, both experimental and wartime, indicate that, although the pulmonary tissue may be severely damaged, the trachea and major

Fig. 6.—Traumatic rupture of the left main bronchus. Note that the tear originates at the carina and involves the cartilaginous portion of the bronchus. The lung parenchyma is intact.

bronchi are not significantly affected. An increase in endobronchial pressure, produced by inflating the isolated lung through the trachea, results in the appearance of numerous small peripheral air leaks from alveolar disruption (Fig. 8). Attempts to tear the bronchi from the trachea with force exerted along the longitudinal axis of the trachea and bronchus requires a force of 11 kg., while a distracting force acting at the carina on the two bronchi simultaneously requires only 3 kg. of tension to produce tearing at or near the carina. The data obtained from the series of experiments indicate that the bronchi are torn at a vulnerable point, rather than exploded, sheared, or crushed.

On the basis of the foregoing experimental effort, a mechanism of injury is suggested.

When blunt trauma is applied to the chest in the anteroposterior diameter, the anteroposterior dimensions of the chest decrease and the transverse dimensions increase. The lungs, owing to the negative intrathoracic pressure, remain coapted to the chest wall, and the two lungs are pulled apart, producing a distracting force at the carina. If the lateral excursion of the lung is carried beyond the point of elasticity of the bronchi, a

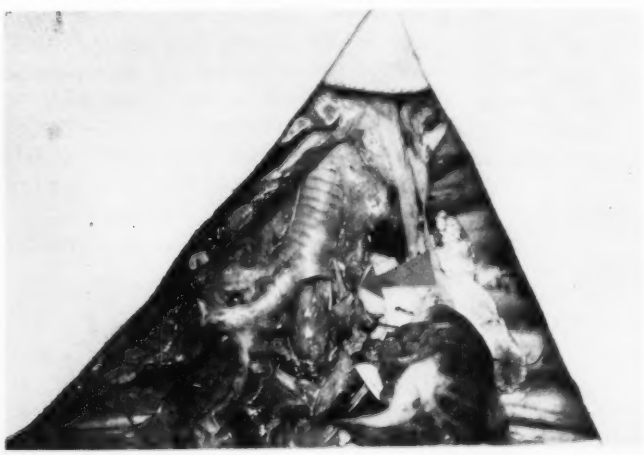


Fig. 7.—The soft tissues overlying the carina have been dissected away, and complete severance of the left main bronchus is shown.

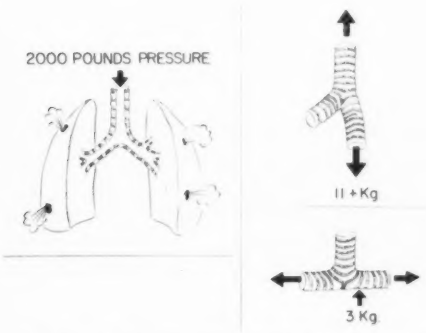


Fig. 8.—Drawings demonstrating (1) the alveolar disruption with explosive inflation of the tracheobronchial tree, and (2) the magnitude of distracting forces required to tear the bronchus while acting in the longitudinal axis of and at right angles to the trachea.

tear results at or near the carina. For instance, a dog's chest 36 in. in circumference will measure 8 to 9 in. in width. At the moment of extreme compression, the transverse diameter will be 14 to 15 in. Thus, an increase of as much as 7 in. may be produced in the transverse diameter. The bronchi of a dog of this size will stretch about 4 or 5 in. before tearing. These figures are consistent with the concept that lateral distraction is of the magnitude to exceed bronchial elasticity. There are several factors involved which tend to augment this distraction of the two bronchi. The anterior chest wall tends to push the lungs apart as it approaches the spinal column, and the heart, insinuated between the lungs, pushes primarily the left lung laterally, and, to a less extent, the right lung. In the dog, x-ray studies demonstrated a severe degree of cardiac displacement in extreme anteroposterior compression of the chest.

These factors become additive when a blow is delivered to the chest in the anteroposterior diameter, and the resultant distraction, acting on the bronchi at the carina produce the tears that have been observed clinically and experimentally.

In addition to the distracting force discussed above, the experimental data indicate that additional factors are involved in rupture of the bronchus.

1. A closed glottis, simulated by a clamped, tight-fitting endotracheal tube in the experimental animal, significantly influences the incidence of bronchial tears. A lung that cannot deflate retains the majority of its bulk, and the lateral displacement of the lung by the heart and the anterior chest wall is enhanced. The combined figures from Series I, Groups 1 and 2, and Series II, Groups 1 and 2, show a 14.3% incidence of rupture of the bronchus with an open airway and a 73.7% incidence of rupture with a closed airway.

2. The width of the object by means of which the chest trauma is induced has apparently a significant influence on the nature of the trauma. When the impact was directed against a broad surface, as in Series I, Group 4, minor mucosal tears resulted; in no instance did the lesion involve the full thickness of the bronchial wall. When a narrow board, 1½ in. wide, was interposed between the chest wall and the source of trauma, major parenchymal damage was done to the lungs, without significant injury to the bronchi. This type of blow produces a wedge-shaped deformity of the chest, with sudden compression of a smaller portion of lung, and tears result. In view of the studies carried out in the presence of a pneumothorax, one might reason that the presence of free air in the pleural cavity as a result of parenchymal tears breaks the negative-pressure seal between lung and chest wall and allows the chest wall to continue in its lateral distortion without the lung.

3. The presence of free air in the pleural space has a very definite effect on the incidence of rupture of the bronchus (Series II, Group 3). Should the nature of the trauma result in a parenchymal tear before the distracting forces acting at the carina have exceeded the bronchial elasticity, the resultant pneumothorax should free the lung from the chest wall and diminish the total distraction applied to the bronchi.

There is probably a critical amount of free air involved in this situation, estimated to be somewhere between 25 and 50 cc. A left-sided pneumothorax of 50 cc. protects the bronchus from rupture, while a right pneumothorax of 50 cc. resulted in tears of the left main bronchus in two of five animals.

4. The force applied to the chest must be of sufficient magnitude to produce extreme anteroposterior compression. In the dog, this minimum force is in the neighborhood of 700 lb., or 15 times the force of gravity. In the average 25 to 30 lb. dog, the anteroposterior thickness of the midthoracic area of the spinal column is about 2¾ in. Arresting the impact as little as ¼ in. above this point prevented significant intrathoracic injuries.

5. While the distracting force acts in such a way as to cause the two main bronchi to be pulled apart, there is an additional factor to be considered, i. e., fixation. The tracheobronchial tree, at the level of the carina, is not solidly fixed, and a pull on one of the bronchi without the factor of fixation may well not exceed the limits of elasticity of the bronchus, owing to a shift of the carina in the direction of the pull.

If all these factors are consolidated, a statement explaining the mechanism of injury may be formulated.

When the chest is compressed in the anteroposterior diameter to an extreme degree, while acting against a closed glottis and inflated lung in the absence of a pneumothorax, the resultant increase in the transverse diameter of the chest and the posterolateral displacement of the heart, plus the factor of fixation of the carina by apposition of the anterior chest wall to the vertebral column, produces a summation of distracting forces acting on the bronchi at right angles to the longitudinal axis of the trachea, which, if exceeding the elasticity of the bronchi, produces a tear in the cartilaginous portion of the bronchus at or near the carina.

Summary

1. Four cases of rupture of the bronchi that have been treated at the Ohio State University Medical Center and one case reported from White Cross Hospital, Columbus, Ohio, are presented.

2. One hundred sixteen cases of rupture of the bronchus have been collected from the literature for the period from 1848 through March, 1957. Five additional cases are added to this number.

3. Rupture of the bronchus has been produced in the experimental animal.

4. A significant factor in the production of the lesion is a distracting force acting on the bronchi at the carina which exceed, bronchial elasticity, augmented by (*a*) a closed airway, (*b*) inflated lungs, (*c*) absence of a pneumothorax, (*d*) the posterolateral displacement of the heart and mediastinal soft tissue, (*e*) an impacting force of sufficient magnitude, (*f*) an area of impact, and (*g*) fixation of the carina by apposition of the sternum and vertebral column.

Dept. of Thoracic Surgery, University Hospital (Dr. Klassen).

DISCUSSION

DR. JACOB K. BERMAN, Indianapolis: I think this is a very important paper. Dr. Lloyd and his associates deserve much credit, particularly for emphasizing the mechanics of these injuries and the liability of major vascular damage.

We have had four patients with ruptured bronchi, and one very unusual case with laceration of the pulmonary artery, which I reported in the *Quarterly Bulletin of the Indiana University Medical Center* under the general heading "Traumatic Avulsions of the Lung and Other Organs Without External Wound." This patient was a 50-year-old woman, a deaf-mute, who was struck by an automobile. Her condition was described as moribund. Her blood pressure was unobtainable, and her pulse was rapid and feeble. There was copious hemoptysis, and x-rays disclosed a hemopneumothorax. Thoracenteses yielded approximately 1000 cc. of blood. She had nonpenetrating fractures of the second, third, fourth, fifth, and sixth ribs on the right side.

We saw the woman 10 weeks later. There was complete opacity of the right side. At operation we found an avulsion of the right main-stem

bronchus about 0.75 cm. from the carina at the site shown by the authors in their Figure 4. The distal end had penetrated the right pulmonary artery. The entire right lung was filled with thick, greenish mucus, and, of course, the lung was immobile and covered with a fibrinous exudate. The proximal end of the bronchus was freed and was found to be completely occluded by scar tissue. The azygos vein was divided and the superior vena cava retracted medially; then Serrefine clamps were applied to the pulmonary artery proximal and distal to the embedded bronchus. The distal end of the bronchus was dissected from the artery, and the vessel was sutured transversally.

We removed almost a complete bloody mucus cast of the right bronchial tree, then washed the bronchus with saline. The two ends of the bronchus were trimmed and anastomosed. No complications or sequelae occurred, and the lung functions normally.

This case illustrates one type of combined major bronchial and vascular laceration.

DR. JAMES R. LLOYD, Columbus, Ohio: I want to thank Dr. Berman for discussing our paper.

We did have film demonstrating some of the actual trauma, but we do not have time to show it.

This problem has been a very interesting one, and I have thoroughly enjoyed presenting it. May I ask Dr. Berman the date of his publication?

DR. JACOB K. BERMAN, Indianapolis: October, 1955.

DR. JAMES R. LLOYD, Columbus, Ohio: I think I may have included this report in my statistics, sir.

Pulmonary Resections for Metastatic Lesions

JOHANN L. EHRENHAFT, M.D.; MONTAGUE S. LAWRENCE, M.D., and DAVID M. SENSENIG, M.D., Iowa City

The thought that a localized metastasis in the lungs may represent the only tumor remaining in the patient has led surgeons to carry out pulmonary resections with some expectation of cure in an otherwise hopeless disease. Even if the patient eventually dies of his disease, prolongation of life or relief of any distressing symptoms may be achieved. There has been considerable difference of opinion regarding the advisability of this course of action. Certainly the low mortality of pulmonary resection should not encourage the use of a futile operation. Therefore, periodic reevaluation of results is certainly indicated to enable us to state with more accuracy whether or not such surgical intervention is justified.

A previous report of nine patients by one of us (J. L. E.)[1] was preceded by publications on the same subject by Seiler, Clagett, and McDonald[4] and by Eschapasse.[2] The latest, and by far the most extensive, review of the literature and the report of an additional 29 cases by Gliedman and associates[3] has brought the total number of cases in the literature to 264. The present report gives the results in 37 additional cases, including the previous 9 reported in which resection for proved metastatic pulmonary malignancy was carried out. The data cover the period from Jan. 1, 1946, to Dec. 31, 1957 (Table 1).

We have followed three criteria for the selection of patients in this series.

1. The apparently complete removal of the primary extrapulmonary neoplasm without evidence of local recurrence

2. The absence of demonstrable metastases to other organs of the body

3. Evidence that all metastases are located in such a manner as to permit their complete surgical removal, even though this may at times necessitate multiple or bilateral pulmonary resections.

Fifty-five selected patients met the criteria of metastatic malignancy as shown by careful histopathologic study. All patients in whom the possibility of a primary pulmonary neoplasm existed were excluded. Of the total of 55 patients subjected to exploratory thoracotomy, it was possible to remove the pulmonary metastases in 37. Twenty-eight of those resections were for metastatic carcinoma and the remaining nine for sarcoma. In the group of 18 patients found to have nonresectable lesions, 15 had carcinoma and 3 sarcoma.

The average age for all patients in whom pulmonary resections were performed was 56.3 years in the carcinoma group and 37.8 years in the sarcoma group. The length of time between treatment of the primary extrapulmonary neoplasm and the exploratory thoracotomy could be established in only 37 patients with carcinoma. It ranged from 0 to 240 months, with an average of 59 months. In 12 patients with sarcomatous lesions the range was 7 to 255 months, with an average of 71 months. In this series there seems to be no correlation of the time between treatments of the primary and secondary lesions and the salvage of patients. The longest interval between treatment of the primary lesion and treatment for the pulmonary metastases was in patients with carcinoma of the breast. The average time was 97 months, with a range of 21 to 240 months. In this group exploration was done in 10 patients, but in only 3 could the metastasis be removed. All of these 10 patients have died of their disease

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From the Department of Surgery, State University of Iowa College of Medicine.

Read at the 15th Annual Assembly of the Central Surgical Association, Columbus, Ohio, Feb. 22, 1958.

TABLE 1.—*Summary of Pulmonary Resections for Metastatic Lesions* *

Case	Primary Lesion	Operation	Time (Mo.) from Treatment of Primary Lesion to Pulmonary Resection	Months After Pulmonary Resection		
				Alive	Until Death	Cause of Death
1	Adenocarcinoma breast	Pneumonectomy	37		14	Recurrent tumor
2	Adenocarcinoma breast	Lobectomy	41		8	Recurrent tumor
3	Adenocarcinoma breast	Pneumonectomy	21		9	Recurrent tumor
4	Epidermoid carcinoma cervix	Pneumonectomy	23	5		
5	Epidermoid carcinoma cervix	Pneumonectomy	72		16	Recurrent tumor
6	Adenocarcinoma cervix	Pneumonectomy	110		0	Operative hemorrhage
7	Adenocarcinoma uterus	Pneumonectomy	36		2	Recurrent tumor
8	Adenocarcinoma uterus	Pneumonectomy	25		0	Postoperative pulmonary embolus
9	Adenocarcinoma uterus	Pneumonectomy	136	22		
10	Adenocarcinoma uterus	Lobectomy and segmental resection	84		12	Cerebrovascular accident (autopsy, no tumor found)
11	Epidermoid carcinoma nasopharynx	Wedge resection	26		24	Recurrent tumor
12	Epidermoid carcinoma lip	Pneumonectomy	36		0	Cardiac arrest during operation
13	Adenocarcinoma stomach	Lobectomy	72		33	Recurrent tumor
14	Adenocarcinoma colon	Lobectomy	36		12	Recurrent tumor
15	Adenocarcinoma colon	Lobectomy	72		17	Coronary occlusion (autopsy, no tumor found)
16	Adenocarcinoma colon	Lobectomy	49	26		
17	Adenocarcinoma colon	Pneumonectomy	65		29	Recurrent tumor
18	Adenocarcinoma colon	Pneumonectomy	5		26	Recurrent tumor
19	Adenocarcinoma colon	Wedge	2	4		
20	Adenocarcinoma rectum	Pneumonectomy	21		8	Recurrent tumor
21	Adenocarcinoma (?) prostate	Lobectomy	?	21		
22	Hypernephroma	Segmental	17		4	Recurrent tumor
23	Hypernephroma	Lobectomy	2	13		
24	Hypernephroma	Segmental resection	8		5	Recurrent tumor
25	Hypernephroma (?)	Wedge	?		18	Recurrent tumor
26	Transitional-cell carcinoma bladder	Pneumonectomy	61		13	Recurrent tumor
27	Embryonal-cell carcinoma, testis	Wedge	10	86		
28	Embryonal-cell carcinoma, testis	Wedge, left Lobectomy, right	11 16	36 31		
29	Cystosarcoma phyllodes, breast bilateral	Wedge, left Wedge, right	60 36	12 7		
30	Leiomyosarcoma, retroperitoneal	Wedge, left Wedge, left	9 1	3 2		
31	Leiomyosarcoma uterus	Local excision, left Wedge, right	48 46		24	Recurrent tumor
32	Osteogenic sarcoma femur	Lobectomy	255		4	Recurrent tumor
33	Fibrosarcoma ankle	Pneumonectomy	60		13	Recurrent tumor
34	Fibrosarcoma tibia	Lobectomy	7		18	Recurrent tumor
35	Granular-cell myoblastoma thigh	Segmental, right Segmental, left Segmental, right	75 123 133	65		
36	Melanosarcoma face	Lobectomy	10		6	Recurrent tumor
37	Melanosarcoma nasopharynx	Segmental	16		47	Recurrent tumor

* Compiled Dec. 31, 1957.

within two years except one, who is still alive, less than six months after exploratory thoracotomy alone. In the group of patients with sarcomatous pulmonary metastases also no correlation could be established. Some of the patients with the longest interval between treatment of the primary extrapulmonary lesion and treatment for the pulmonary metastasis were found to have nonresectable metastatic involvement or their survival after pulmonary resection was not prolonged. In 37 patients various

TABLE 2.—*Pulmonary Resections*
(37 Patients)

Unilateral	30
Bilateral	5
Multiple unilateral	1
Multiple bilateral	1

TABLE 3.—*Type of Operation*
(37 Patients)

Pneumonectomy	14
Lobectomy	12
Segmental and wedge	17
Second exploration	2

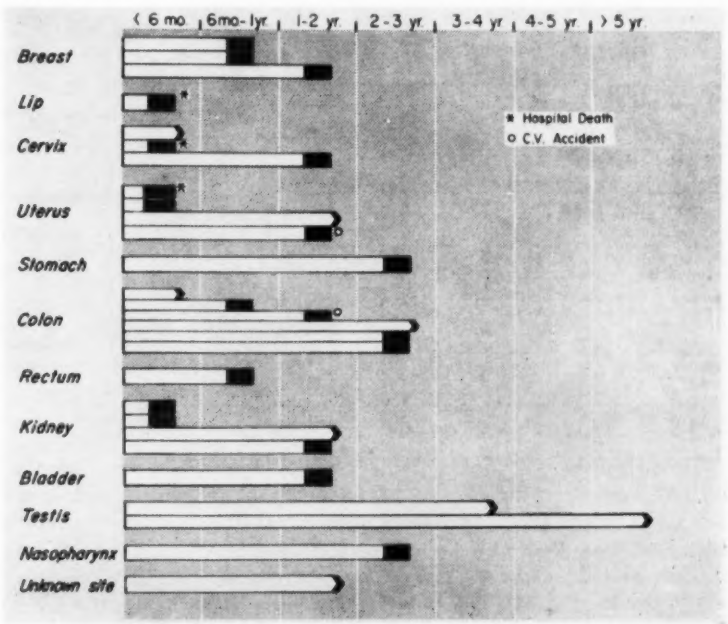
types, and at times bilateral and multiple resections, were performed (Table 2).

The site of the primary extrapulmonary malignancy was unknown in three patients who were subjected to exploratory thoracotomy and in one patient who had resection of a pulmonary metastasis.

Of the resections, 14 were pneumonectomies, 12 were lobectomies, and 17 were segmental or wedge resections. Two patients were subjected to a second exploratory thoracotomy after a previous resection, and in neither was the lesion resectable (Table 3). There were 3 deaths in 43 resections in 37 patients, but no patient died after exploratory thoracotomy alone. All the deaths followed pneumonectomy for metastatic carcinoma. One patient died of cardiac arrest during operation; one as a result of operative hemorrhage, and the third seven days postoperatively of a pulmonary embolus.

Among the 28 patients undergoing resection for metastatic carcinoma there are 8 survivors as of Dec. 31, 1957, without evidence of recurrence. Their postoperative survival periods are 4, 5, 13, 21, 22, 26, 36, and 86 months (Fig. 1). Among the nine patients with sarcoma, there are three survivors without recurrence 3, 7, and 65 months after operation (Fig. 2). Thus 21% have survived over one year in the carcinoma group and 11% over one year in the sarcoma group. Although the number of patients involved is small, the figures do not give the impression that the results

Fig. 1.—Survival periods for 28 patients with metastatic carcinoma undergoing exploration and resection.



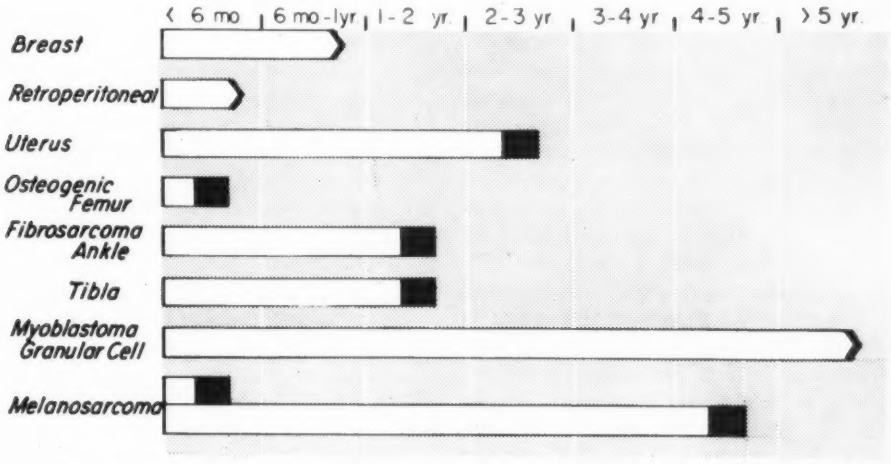


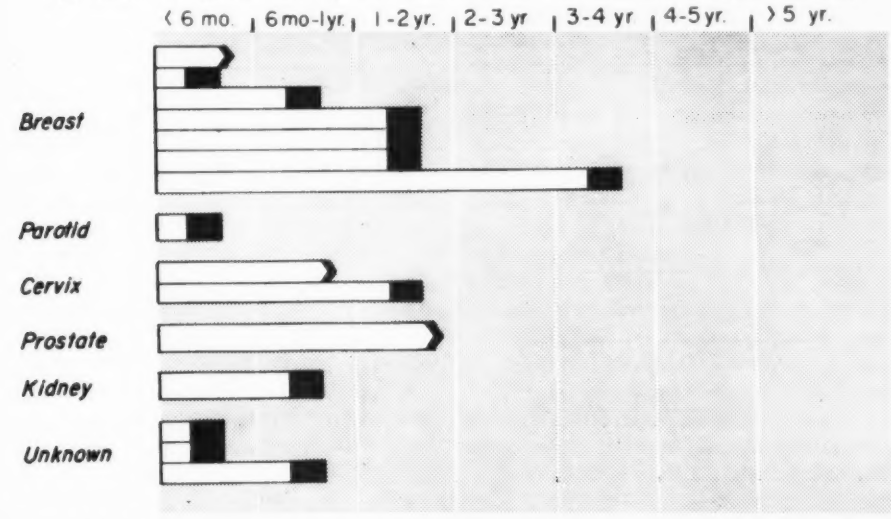
Fig. 2.—Survival periods for nine patients with metastatic sarcoma undergoing resection.

are better among the patients with metastatic sarcoma than among those with metastatic carcinoma, as found in the data collected from the literature.[3]

Of the 28 patients undergoing resection in the carcinoma group, 3 patients are alive two years after operation. It is of interest to note that the patients with the longest survivals, three and seven years, respectively, were young men whose primary lesion was a chorioepithelioma of the testis. One patient whose primary lesion was a carcinoma of the uterus, and a second, whose primary neoplasm was a carcinoma of the colon, died of cardiovascular accidents between the first and the second year following pulmonary resection. At the time of autopsy no residual tumor was encountered in either patient.

In the group of 15 patients with carcinoma in whom only exploratory thoracotomy was performed, 3 patients are alive,

Fig. 3.—Survival periods for 15 patients with metastatic carcinoma not undergoing resection.



less than two years after operation, while all others have died of their disease. These deaths occurred within two years, with one exception, that of a patient with carcinoma of the breast who survived over three years (Fig. 3). Of the nine patients in whom metastatic pulmonary sarcoma was resected, three are alive. For two of these the survival is still less than two years. One of these is a patient with cystosarcoma phyllodes of both breasts who was subjected to bilateral wedge resection. The other is a 14-year-old girl who was treated with wedge resections on the same side on two separate occasions for metastatic leiomyosarcoma originating in the retroperitoneal space. One patient who is still alive, over five years since the first resection, has had multiple bilateral segmental and wedge resections for metastatic granular-cell myoblastoma originating in the thigh.

All of the three patients subjected to exploratory thoracotomy without resection in the sarcoma group died of their disease within four months.

If distressing pulmonary symptoms were relieved, the operation would appear to be justified, even though prolonged survival following removal of pulmonary metastatic neoplasms was not obtained. Severe and crippling pulmonary osteoarthropathy was encountered in two patients with carcinoma and in two with sarcoma. This symptom was dramatically relieved in all by removal of the pulmonary metastasis.

We have found that metastatic carcinoma may invade a bronchus and metastasize to lymph nodes like a primary pulmonary tumor. Of 28 patients in whom pulmonary resections for metastatic carcinoma were carried out, 7 had presented endobronchial invasion. Positive preoperative bronchoscopic biopsy specimens were obtained in four. In eight patients of this group the surgical specimens contained regional or hilar lymph nodes involved by metastatic carcinoma. In contrast, no endobronchial or regional lymph node involvement was encountered in nine patients who had resections for sarcomatous lesions.

The time of appearance of a pulmonary metastasis following resection of a primary extrapulmonary lesion seems to be of less importance than the type of tumor and its biologic behavior. As mentioned above, the results in carcinoma of the breast have been very discouraging in our experience, and it may indicate that pulmonary resections for metastatic breast carcinoma should not be performed. In the patients with carcinoma of the testis, which is regarded as a highly malignant tumor, the time intervals were 10 and 16 months. Both these patients are still alive, seven and three years respectively, without evidence of recurrent neoplasm.

In the group of patients who underwent operation for metastatic sarcoma, the late appearance of a pulmonary metastasis after treatment of the primary lesion again does not seem to have any influence on the prolongation of life and salvage of the patient. For example, one patient with osteogenic sarcoma underwent exploration after an interval of 156 months and was found to have an inoperable tumor. He died of his disease in two months. Another patient with the same type of neoplasm underwent pulmonary resection 21 years and 3 months following the initial hip disarticulation for a lesion in the femur. This patient died of his disease four months after the pulmonary resection.

Comment

The rich capillary bed of the lung constitutes a filter which may bring about localization of tumor emboli. Whenever these tumor emboli establish themselves in the host tissue, and many do not, they may progress to a state where multiple metastases in the lung parenchyma can be demonstrated early by radiographic means. For this reason, in a vast majority of patients malignant pulmonary metastases of extrapulmonary origin do not represent a surgical problem. However, the presence of larger, and at times solitary, metastatic lesions are therefore of greater significance from the surgical point of view.

The knowledge of a preexisting extrapulmonary neoplasm previously treated makes the diagnosis of metastatic pulmonary deposits much more likely. However, one must always consider the possibility of a second primary neoplasm arising in the lung. The symptoms and clinical behavior of lesions metastatic to the lung not infrequently simulate closely the clinical picture of primary bronchogenic neoplasms. This is more likely in case of metastatic carcinoma than of sarcoma.

Metastatic lesions in the lung may appear months, and at times many years, after complete removal of the primary extrapulmonary tumor. Less frequently a solitary pulmonary metastasis is present at the time of surgical extirpation of the primary extrapulmonary neoplasm. When the pulmonary lesion and the primary malignant tumor are found simultaneously, the problem is always more complex.

Adhering to our indications for resection given above, we have found that in this otherwise hopeless group of patients a small percentage will be cured of their disease and others will receive palliation of distressing symptoms.

From the available data there is no indication that salvage of the patient is related to the type of pulmonary resection. There are survivals in every group, and our present policy is to remove only as much lung tissue as is necessary to encompass the lesion. We believe limited resections are preferable, especially in view of the fact that multiple operations may be indicated.

It is interesting that in our series of patients there is no correlation of the length of time between treatment of the primary lesion and the appearance of pulmonary metastatic disease and salvage of the patient. A long interval is not necessarily associated with an increased survival rate.

The biologic behavior of the tumor is probably the most important factor. The results of surgical treatment of metastatic pulmonary breast cancer were so discouraging that it appears that pulmonary resection is not justified.

Summary and Conclusions

The results of surgical treatment of proved metastatic pulmonary malignancy at the University Hospitals, State University of Iowa, are reviewed.

Fifty-five patients underwent exploratory thoracotomy. Pulmonary resections were carried out in 37, being for carcinoma in 28 patients and for sarcoma in 9.

In the group of patients who had resections for carcinoma, three are alive, from two to seven years postoperatively. Of 15 patients undergoing exploration but without resection, three are alive, from one to two years since operation.

In the group of patients who had resections for sarcoma, one patient is alive, five years following operation. All three patients with metastatic sarcoma who had exploration but not resection died within four months.

Worthwhile palliation can be achieved by pulmonary resection of metastatic lesions.

Although this complex problem needs periodic reporting of results, it is our belief that resection of metastatic pulmonary malignancy is indicated in carefully selected patients.

Department of Surgery, State University of Iowa College of Medicine.

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DISCUSSION

DR. NEIL C. ANDREWS, Columbus, Ohio: Dr. Ehrenhaft very kindly asked me to discuss this paper.

We have had an experience with 24 patients with metastatic lesions at the Ohio State University,

most of these patients being treated on Dr. Klassen's service.

Our sarcoma group is a little larger than the authors', comprising 13 sarcomas, as against 11 of theirs. In this group of 24 patients 5 lived at least five years; 2 of these 5 died shortly thereafter the survey; 2 lived at least three years and are still alive.

In evaluating these cases, we have found that there appears to be no relationship between survival and the time of the resection of the primary malignancy and the discovery of the metastatic lesion. One thing we feel should be done in the preoperative work-up of these patients is laminography. Only rarely is bilateral resection justified, and laminography may show a second lesion that will indicate that resection should not be carried out.

DR. DAVID M. SENSENIG, Iowa City: I would like to thank Dr. Andrews for his interesting comments. The rich capillary bed of the lung constitutes a filter in which tumor emboli may localize. Many of these do not. Frequently, of course, there are multiple metastases, and it is only the larger, and at times solitary, lesions that are of importance from the surgical point of view.

Implant Radiation Therapy for Carcinoma of the Pancreas

PAUL V. HARPER, M.D., and KATHERINE LATHROP, M.S., Chicago

An increasing number of five-year survivals following radical surgical treatment of carcinoma of the head of the pancreas are appearing in the literature,[1] so that serious consideration must be given to this form of treatment in favorable cases. However, unfavorable or technically inoperable cases probably still constitute the majority of carcinomas in this region as they are encountered clinically, and for this group of cases we must seek other forms of therapy. Treatment in these cases has been limited for the most part to bypass operations to remove obstruction. Radiation therapy for these inoperable tumors has been attempted with some success where local implant therapy was used with radium or radon, with or without external irradiation.[2] There are, however, certain severe limitations in this approach in that the radioactive sources must be available at the time of operation, the operator must accept substantial radiation exposure during the procedure, and the radiation sources in the cases of radium needles must be removed, a somewhat difficult and dangerous procedure inside the abdomen. While a number of ways have been devised to circumvent these difficulties, a very flexible and generally applicable approach has been that of using a linear gamma-ray source consisting of fine polyethylene tubing filled with a solution of gamma-ray-emitting isotope. The implant is constructed by sewing the tubing around and through the tumor, following as closely as possible the Paterson-Parker distribution rules. Both ends of the tubing are brought out through the skin, and subsequently, when the patient has recovered from the surgical procedure, the tubing is filled with isotope solution to produce a localized radiation field in the region of the implanted tumor. Previous experiences[3,4] with this technique are amplified in the present report.

During the past several years, our previously reported technique has undergone some minor changes, and at the present time we follow the procedure outlined below. In performing the implant, polyethylene tubing (Clay-Adams PE-10; outer diameter 0.61 mm., inner diameter 0.28 mm.) is used. This is about the same size as 0 absorbable surgical (gut) suture. The tubing is kept sterile and available at all times in the operating room. Either 70% alcohol or benzalkonium (Zephiran) is a satisfactory sterilizing agent. Using ordinary needles of various sizes, the tubing is threaded around and through the tumor, following as closely as possible the Paterson-Parker distribution rules. For a roughly spherical implant three-fourths of the tubing is evenly distributed on the periphery of the tumor and one-fourth spaced evenly through the volume. The tubing is spaced approximately 1 cm. between turns, and careful measurements are made of the length of the tubing comprising the implant and of the ends leading from it. The ends of the tubing are brought out through the wound and left long. The tubing is easy to handle in 6- or 8-ft. lengths at the operating table and has very little tendency to kink or tangle. Care must be taken during the

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From the Argonne Cancer Research Hospital (U. S. A. E. C.) and the Department of Surgery, University of Chicago.

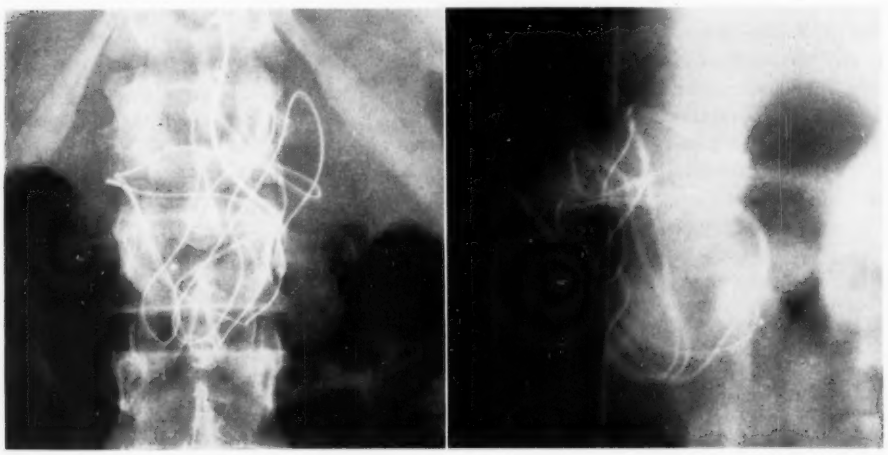
procedure to prevent blood or serum from entering the lumen of the tubing, where it may clot and cause obstruction. During the procedure the tumor is disturbed and handled as little as possible to avoid dissemination of tumor cells. The tubing may be filled with mercury and the distribution checked roentgenographically before closing the abdomen. As there is no radiation present during this part of the procedure, it is possible to perform a careful, painstaking placement of the implant without exposure of the operator to ionizing radiation. Nearby vulnerable organs may be displaced surgically away from the implant to whatever extent is feasible, and the omentum may be interposed. The radiation field falls to one-half or less of that within the implant at a distance of 1 cm., so that even a small displacement of the stomach, colon, or small intestine is very valuable. This permits the radiation dose in the implant to be increased by a factor of 2 or more over that which can be tolerated with external irradiation, where the dose must necessarily be limited by the tolerance by the bowel wall of 5000 or 6000 r.

After the implant is made, the patient is allowed to recover from the operation to whatever extent is necessary. Steps are taken to procure the desired isotope, or, if necessary, the patient may be sent to another institution for administration of the isotope.

In preparation for administration of the isotope, the tubing is cleaned with distilled water, dried with alcohol and ether, and then filled with mercury. Roentgenograms are then taken, and from these the volume of tissue to be irradiated in the implant can be measured and the quantity of isotope desired can be calculated. The accompanying Figure shows such an implant in the head of the pancreas with the tubing filled with mercury for purposes of radiography.

In all our patients so far we have used the gamma radiation from I^{131} to produce the radiation field. The gamma-ray dose from 1 mc. of I^{131}, decaying completely, corresponds to 75 mg-hr. of radium. Using this factor, it is possible to calculate from the Paterson-Parker volume implant tables the quantity of I^{131} necessary to produce any desired radiation dosage in the implant. Other isotopes than I^{131} may be used, but at the present time this isotope still appears to be the most satisfactory because of its availability, cheapness, and suitable chemical and physical properties.

Anteroposterior (left) and lateral (right) roentgenograms of an implant with mercury in tubing (Case 13). Location: head of pancreas. Volume: 54 cc. Quantity of isotope: 88 mc. Radiation dose: 13,600 r. Result: freedom from pain for six months.



To prepare the iodine for administration, a quantity 20% in excess of the required amount in a 2 to 10 cc. volume is placed in a conical centrifuge tube. One or two milligrams of potassium iodide is added as carrier, and the iodine is precipitated quantitatively as silver iodide with a slight excess of silver nitrate. The solution is acidified with nitric acid, digested at 70 C for an hour to flocculate the precipitate, and then centrifuged. The supernatant is decanted, and the precipitated silver iodide is dried in the stream of air in the dark at room temperature. The supernatant is surveyed to check for the completeness of precipitation, which is usually about 99%. The centrifuge tube containing the isotope is handled at all times in a lead-shielded container to minimize exposure. The total body exposure to the operator determined by a pocket dosimeter during the processing of 200 mc. of I^{131} without taking extraordinary precautions was 7 mr.

The silver iodide is prepared for placement in the implant by dissolving it in a sufficient volume of saturated potassium iodide to give the correct number of millicuries per centimeter of tubing. This is accomplished with sufficient accuracy by filling an appropriate length of polyethylene tubing of the same size as is used in the implant with saturated potassium iodide and discharging it onto the silver iodide precipitate, which dissolves readily.

The dissolved silver iodide is then drawn up into polyethylene tubing, forming a column of solution equal in length to the tubing in the implant. Preceding and following this column of isotope solution are columns of inactive potassium iodide solution equal in length to the tubing running between the implant and the point of exit of this tubing from the body. Separating the potassium iodide from the isotope solution at each end is a 1 cm. bubble of air. This tubing, containing the solutions as described, is then placed in a lead pot with both ends protruding and in this form is transported to the patient's bedside.

The mercury in the implant is then removed, and the tubing is cleaned of all traces of mercury by rinsing briefly with concentrated nitric acid, then with distilled water, alcohol, and ether, and drying with air.

The tubing in the lead pot containing the isotope solution is then connected to the tubing as it enters the patient's body, using a No. 27 needle with the hub broken off as an adapter. The isotope is then displaced with mercury from the tubing in the lead pot into the tubing in the implant, so that in the final situation the column of isotope solution is in the implant and the tubing leading from the implant to the surface of the body is filled with inert potassium iodide solution. When this procedure is used, the residual activity in the tubing through which the isotope solution has passed is extremely slight, and there is no mercury within the tubing inside the body, as there was with our previously reported technique. The presence of mercury was found to be undesirable, because it reacts slowly with the iodide solution, producing crystals which occlude the lumen of the tubing after several days or weeks.

The quantity of isotope administered is checked by drawing up a small quantity of the residual solution of silver iodide into polyethylene tubing, measuring the length of the column of solution in the tubing, and then diluting it and counting an aliquot under conditions of known geometry. This gives a direct measure of the number of millicuries per centimeter of tubing.

When the treatment has been completed and the decision is made that it will be unnecessary either to give more isotope solution or to remove the isotope solution that is present, the ends of the tubing are sealed off and allowed to retract beneath the skin and the tubing is left in place permanently.

The advantages of this method, as pointed out above, are that all radiation hazard to the operator is eliminated; the need for prior planning is also largely eliminated.

so that an unexpected situation may be taken care of in the operating room, the only requirement being that sterile tubing be kept on hand. The isotope need not be placed in the implant for days or weeks after the operation, so that it is unnecessary to have the isotope immediately available. Indeed, the procedure could well be carried out at a small hospital, and the patient subsequently sent to a medical center for administration of the isotope if this were necessary. If the patient should die with significant amounts of radioactivity in his body, one can remove the isotope from the tubing and thus avoid considerable difficulties for the pathologist and undertaker. The limitations of this approach are the same as those of any form of implant therapy, although the somewhat lower dose rate appears to permit a higher general tolerance than would be expected from radium or radon. Thus the maximum size of the tumor that can be treated successfully is of the order of 100 gm., or, on the other hand, the amount of isotope which may be given safely is about 150 mc.

During the past five years, we have attempted this procedure in 14 patients and carried it out successfully in 12. Our experiences with these patients are summarized in the following case reports. The dose values for the early patients have been recalculated, using a more precise estimate of the divergent distortion in the roentgenogram of the implant, so that these figures are 20% to 30% higher than those previously reported. In all cases except Case 12, the malignancy was histologically verified.

Report of Cases

CASE 1.—This 56-year-old man had a 150 gm. tumor of the body of the pancreas, which was first discovered at operation. This was implanted with tubing, and in the process the hepatic artery was perforated twice. The tubing was withdrawn from the hepatic artery, and bleeding ceased promptly. There were no apparent ill effects. A cholecystogastrostomy was performed. The patient at first did well after the operation, but soon became severely depressed, refused to eat, and finally died of inanition, three weeks after the operation. No autopsy was obtained, and no isotope had been placed in the tubing.

CASE 2.—This 55-year-old woman had a mass in the pancreas, which was discovered in May, 1953, during cholecystectomy. A reexploration was done in August, 1953, for continued back and epigastric pain, and the tumor was found to have extended around the root of the mesentery. Exploration was again carried out at this hospital on Nov. 5, 1953. At operation a large tumor, weighing about 89 gm., in the head and body of the pancreas was implanted with tubing. It was impossible to place the core of the implant symmetrically because the superior mesenteric artery and portal vein traversed the implant. The common duct was transplanted to the greater curvature of the duodenum, and the pylorus was transected and an anterior gastroenterostomy was performed, allowing the stomach to be displaced to the left side of the abdomen, away from the implant. One week after operation, 135 mc. of I^{131} was placed in the tubing. This gave a calculated dose of about 6500 r to the lowest point in the implant and an average dose of 17,300 r over the whole implant. The patient tolerated this well, without evidence of radiation sickness, and her appetite remained good. Four weeks after isotope administration she developed a severe anemia (hemoglobin 8.0 gm. %), and leukopenia (leukocyte count 1900 per cubic millimeter). This responded during the next three months to repeated transfusions and supportive therapy. The patient's epigastric pain and back pain were much improved, so that she was able to discontinue completely the use of narcotics. Her tumor mass decreased slightly in size, and the skin over it became tanned from the radiation coming outward from the implant. Six months after treatment she began to fail, and numerous abdominal masses became palpable. The patient became severely jaundiced and died on June 8, 1954. No autopsy was obtained.

CASE 3.—This 66-year-old woman had a history of back pain, weight loss, and anorexia for nine months and of moderate obstructive jaundice for two weeks. An exploration was done on Dec. 5, 1953, and a small tumor (9 gm.) of the pancreas or distal part of the common duct was implanted with polyethylene tubing. The common duct was transplanted to the greater curvature of the duodenum to relieve the obstruction. On Dec. 10, radioactive iodine, 10.6 mc., was placed in the tubing, and five days later this was removed and replaced with 21.3 mc., which gave a calculated total radiation dose of 14,500 r. The patient's jaundice disappeared, but she continued to have pains in her back. She did fairly well for three months, and there was no apparent adverse effect from the radiation. She was hospitalized again on Jan. 9,

1954, when she complained of nausea and vomiting. Roentgenograms of the duodenum adjacent to the implant did not reveal any abnormal condition. Further studies revealed a marked uremia. The patient died on March 23, 1954. At autopsy the cause of death was attributed to chronic pyelonephritis. Grossly, there was little evidence of tumor, but microscopic studies revealed that the carcinoma was invading the peripancreatic tissues. In the region of the implant the tumor showed marked regression, and there was some evidence of fibrosis in the duodenum adjacent to the implant.

CASE 4.—This 42-year-old man gave a five-month history of abdominal and back pain and a 50 lb. weight loss. The character of his stools had changed to an oily, amber liquid, which frequently floated on top of the water. Physical examination was not remarkable. Laboratory data showed 1+ reduction in the urine, and the glucose tolerance curve was markedly diabetic. Roentgenograms were negative. On Feb. 1, 1954, an exploratory laparotomy was done, at which time a carcinoma was found that involved almost the entire pancreas and the surrounding tissues. There were some local lymph node involvement and a few small metastases to the undersurface of the liver. A gastrojejunostomy, cholecystoduodenostomy, and splanchnicectomy were done, and the tumor was implanted with polyethylene tubing. The patient made an uneventful recovery, and 176 mc. of radioactive iodine was placed in the tubing on Feb. 11. The radiation dose in the implant was difficult to estimate because of the peculiar elongated shape of the tumor. The volume was estimated at about 87.5 cc. and the radiation dose at about 13,200 r. The patient was discharged on Feb. 19, and returned to work three weeks later. His back pain was nearly gone, and his only complaints were persistent diarrhea and inability to gain weight. Four weeks after isotope administration he developed marked leukopenia and anemia, which required no particular treatment and regressed spontaneously. He continued to do well until about May 1, when he was readmitted for splanchnic block therapy because of recurrence of pain. At this time, a hard mass was palpable in the epigastrium. Splanchnic block gave some relief from pain. The patient died suddenly on June 19, 1954. Autopsy revealed a large tumor mass in the region of the pancreas, with extensive spread to the liver and the gastrocolic omentum. There was not much evidence of regression of the tumor from the radiation, and there was no apparent damage to any of the other intra-abdominal structures. The portal vein was patent. There was no apparent reason for the sudden cause of death.

CASE 5.—This 50-year-old man had a carcinoma of the head of the pancreas, which was discovered at laparotomy. The pancreas at this time was extensively mobilized, and cholecystojejunostomy was performed. Four weeks later a reexploration was done at this hospital. The operation presented extreme technical difficulty because of the extensive fresh adhesions from the previous operation. While the pancreas was being mobilized, the portal vein was torn, and the resulting hemorrhage could not be controlled. The patient died, and autopsy was not obtained.

CASE 6.—This 59-year-old man complained of severe burning abdominal pain for one year and loss of 25 lb. in the six months prior to admission. He had also recently developed steatorrhea, and in the course of his work-up he was found to be diabetic. Physical examination was otherwise negative, and roentgenograms revealed a pyloric lesion of undetermined nature. On May 21, 1954, an exploration was done, and a large tumor mass, of about 80.5 gm., was found in the head of the pancreas. Anterior gastrojejunostomy following transection of the pylorus, choledochojejunostomy, and cholecystectomy were performed, and the tumor was implanted with polyethylene tubing. After this operation the patient became jaundiced and a reexploration was done one week later, at which time an obstruction of the choledochojejunostomy was found, caused by inspissated bile. This was relieved, and a transjejunal catheter was left in the common duct. The patient made a good recovery from the second operation except for a slight wound dehiscence, and 97.3 mc. of radioactive iodine was placed in the implant on June 2, giving a total dose of 12,500 r. The core of this implant was displaced somewhat by the portal vein and superior mesenteric vessels. The patient got along fairly well and did not show evidence of radiation sickness. He developed leukopenia (leukocyte count 1900) four weeks after the administration of the isotope, which was transient.

After removal of the common duct catheter, one month after operation, a persistent jejunal fistula remained, which subsequently communicated with the opening in the abdominal wound. The patient had several febrile episodes that responded to sulfisoxazole (Gantrisin) and were interpreted as being caused by cholangitis. He gradually became weaker and became jaundiced on Aug. 14 and died on Aug. 16, 1954. Throughout his postoperative course he was free from pain. Autopsy revealed regression of the tumor, although it was not possible to separate the radiation effect from the spontaneous regression characteristic of these sclerosing, mucus-secreting tumors. There was no evidence of further spread or radiation damage to other organs. The fistula from the jejunum communicated with the implant, which was infected, and the cause of death was a septic thrombophlebitis of the portal vein.

Case 7.—This 49-year-old woman complained of weakness for three months, a 20 lb. weight loss in the previous two months, anorexia for six weeks, and increasing jaundice for six weeks. Physical examination was negative except for jaundice, and laboratory examination revealed an obstructive type of jaundice. On July 2, 1954, exploration was carried out, and a 22 gm. carcinoma of the distal common duct or pancreas was found. Gastrojejunostomy and cholecystojejunostomy were performed, and the tumor mass was implanted with polyethylene tubing. The patient made a rapid recovery, and 28.5 mc. of radioactive iodine was placed in the tubing in July, 1954, giving a total dose of 10,800 r. She had no adverse effect from the irradiation and did well until the beginning of February, 1955, when she developed abdominal pain, nausea, vomiting, and chills. On exploration, on March 29, 1955, a bile peritonitis was found, resulting from a ruptured liver abscess. The tumor had implanted itself along the suture line of the cholecystojejunostomy, which was revised, and there was no apparent change in the appearance of the primary tumor. The patient did well in the immediate postoperative period, but then began to weaken, ran a febrile course, which did not respond to antibiotics, and gradually failed, and died on May 8, 1955. Autopsy revealed the cause of death to be cholangitis with multiple liver abscesses. There was no evidence of much damage to the primary tumor from the radiation field of the implant.

Case 8.—This 73-year-old man began having abdominal pain in October, 1953, developed jaundice in December, 1953, and in June, 1954, was seen in another clinic, where a tumor of the pancreas was diagnosed. On Aug. 25, 1954, exploration was done in another hospital, and a tumor in the head of the pancreas, weighing about 16 gm., was implanted with polyethylene tubing. The patient recovered well and was transferred to the University of Chicago Clinics, where 30 mc. of I^{131} was placed in the implant on Sept. 21, giving a calculated dose of 11,750 r in the tumor. The patient, who left the hospital immediately, had no reaction whatever to the radiation therapy. He did moderately well until December, 1954, when he began losing weight, and he died in February, 1955. No autopsy was obtained.

Case 9.—This 66-year-old man, after feeling poorly and anorexic for several months, became jaundiced on Sept. 23, 1954. On Oct. 1, an exploratory laparotomy in another hospital showed a large carcinoma of the head and body of the pancreas, which was implanted with polyethylene tubing. He was admitted to the University of Chicago Clinics on Nov. 10, having recovered from the laparotomy. Measurements indicated an implant volume of 56 cc., and 71 mc. of I^{131} was introduced into the tubing, giving a calculated radiation dose of 10,400 r. The patient had no adverse effect from this radiation and did well until about March 1, 1955, at which time he rather rapidly lost his appetite; his course was downhill, and he died on March 21.

Case 10.—This 62-year-old man had been suffering for 10 months from increasing epigastric pain, made worse by lying down. During this period he had several bouts of vomiting and lost some 60 lb. Exploratory laparotomy on April 13, 1956, revealed a small chronic gastric ulcer on the lesser curvature and a 4×5 cm., stony-hard mass in the body of the pancreas, involving the superior mesenteric artery. Biopsy revealed this mass to be a ductal carcinoma of the pancreas. The tumor was implanted with polyethylene tubing, and the omentum was interposed between the stomach and the pancreas. Because the tumor appeared to involve the third portion of the duodenum to a slight extent, an anterior gastroenterostomy was made. The patient recovered uneventfully from the operative procedure. The volume of the implant determined from the x-ray was 25 cc., and 67 mc. of I^{131} was placed in the tubing, which gave a total dose of 17,200 r. After treatment, the patient's pain was considerably relieved, although not completely, and he got along well, with only minor troubles, until his death, seven months later.

Case 11.—This 51-year-old man had been troubled for three months with epigastric pain radiating to his back, together with a slight diarrhea. During the two weeks prior to admission, he had lost 8 to 10 lb. in weight. He was somewhat jaundiced. Exploratory laparotomy on Sept. 6, 1956, revealed a small, inoperable carcinoma of the head of the pancreas. This diagnosis was confirmed histologically by needle biopsy. Cholecystogastrostomy was performed, and a polyethylene-tubing implant of 8 cc. was made in the tumor. Twenty-three millicuries of I^{131} gave a dose of 11,700 r to the tumor. For two months following treatment the patient did well and was free from pain. He had a moderate diarrhea, which was well controlled with pancreatin. Pain then returned and increased to the point where chordotomy was required; the course was slowly downhill, and the patient died nine months after treatment with the isotope.

Case 12.—This 55-year-old man complained of dull aching pain in the low back, radiating around to the midepigastrium, of one year's duration, and increasing in intensity during the past few months. Five months prior to admission cholecystectomy was performed elsewhere, and no other pathological condition was found in the abdomen. However, his pain continued and increased, and began radiating to the midback, and the patient became nauseated and lost 13 lb. On June 7, 1957, exploratory

laparotomy revealed a carcinoma of the body of the pancreas, which was implanted with tubing, and splenectomy was performed. On June 27, I^{131}, 71.5 mc., was placed in the implant, which had a volume of approximately 23.5 cc. This implant was constructed without a core, so that the dose in the center of the implant was considerably lower than would otherwise be expected. The calculated dose was 8750 r. Approximately a week after the instillation of the isotope, the patient's pain decreased remarkably, and when he was last seen, seven months after the beginning of treatment, the patient had gained 60 lb. and was free from pain and doing well. No biopsy was performed in this case.

CASE 13.—This 68-year-old Negro minister had an eight-month history of abdominal pain, mostly in the upper abdomen, and occasionally radiating to the back. Carcinoma of the pancreas was suspected, and duodenal cytologic study was positive for malignant cells. Retroperitoneal air studies and splenoportography suggested a mass in the pancreas. On June 27, 1957, exploration revealed a large tumor mass in the uncinate process of the pancreas. This was implanted with tubing, and a gastroenterostomy was performed. Subsequently, 88 mc. of I^{131} was placed in the implant, which had a volume of 54 cc., giving a tissue dose of 13,600 r. The white cell count dropped to 2700 per cubic millimeter four weeks later and the hemoglobin to 9.8 gm. %. These values returned to normal without any special therapy. The patient had moderate difficulty with anorexia for a week or two after instillation of the isotope; but this passed, and he gained 10 lb. and continued to do well for six months, at which time his epigastric pain, radiating to the back, returned. At the present time, he has not lost any weight, and his pain is relieved by an acetophenetidin, acetylsalicylic acid, and caffeine preparation (Anacin). His appetite is good.

CASE 14.—This 60-year-old man was admitted with epigastric pain radiating to the back, of one year's duration, and a progressive weight loss of 20 lb. Laparotomy was performed on Oct. 29, 1957, at which time a large mass in the body and tail of the pancreas was discovered. As the tumor was adherent to the lesser curvature of the stomach, this portion of the stomach was resected and the remaining tumor was implanted with polyethylene tubing. On Nov. 6, I^{131}, 82.2 mc., was placed in the implant, whose volume was 70 cc., giving a tissue dose of 10,300 r. The patient tolerated this well, and on Feb. 12, 1958, the isotope was removed and replaced with another mc. of I^{131}.

In considering these cases as a group, remarkably little reaction in terms of radiation sickness was apparent. Anemia secondary to radiation was evident in those patients receiving 100 mc. or more of I^{131}. In almost all the patients in whom pain was a presenting symptom, there was marked or complete relief. Whether this is due to the effect of radiation on the tumor or to the suppression of the secretion in the portions of the pancreas blocked by the tumor is, of course, not clear. In some cases there seemed to be response of the tumor to the radiation, as shown at autopsy, and in others there did not seem to be very much. It is evident that the level of radiation dosage to be effective in these tumors must be quite high. In six of these patients, the portal vein traversed the implant, and this caused no apparent harm except in the case where the implant became infected.

Comment

On the basis of this brief experience with radiation therapy in cases of advanced carcinoma of the pancreas, using the implant technique described, we feel that a high level of local radiation of the order of 10,000 to 15,000 r may be beneficial, and evidently causes very little harm. We feel that one is certainly justified in continuing the exploration of this method in an attempt to find at least a partial solution to this problem. It does not seem feasible to use the implant technique in tumors that are closely adherent to the duodenal wall, or that have invaded the duodenum, because of the danger of causing radiation damage to the duodenum, with subsequent perforation, although in these cases the portion of the duodenum that is in contact with the tumor may be resected in order to remove it from the radiation field. In some cases this appears justified, although it extends the scope of the operation to a considerable extent. On the other hand, it would seem that this technique should be admirably suited to cases of carcinoma of the body of the pancreas in which the anatomy is much less complicated and the results from radical removal extremely poor.

Summary and Conclusion

Our experience with a short series of advanced carcinomas of the pancreas treated with implant therapy at dose levels of 10,000 to 15,000 r indicates that little harm, and a substantial degree of palliation, may be achieved in many cases using this technique.

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DISCUSSION

DR. RICHARD J. IRETON, Columbus, Ohio: I want to compliment Dr. Harper on his ingenious approach to this problem. We have dealt with this problem a few times in the past few years.

(Slide) This is a patient who presented himself to us two weeks after cholecystectomy elsewhere, with obstructive jaundice. At the time of exploration he was found to have a tumor of the head of the pancreas. We could not prove by frozen section that he had liver metastases at that time, and we felt he was in such poor shape that not much surgery could be done. Accordingly, we relieved his jaundice by choledochojejunostomy. We opened the duodenum. Here is the rubber catheter in the ampulla of Vater, this being the side of the duodenum along the head of the pancreas. We inserted thin, hollow needles, six in number, into the pancreas and dropped radioactive gold seeds down these hollow needles. Then we removed each needle approximately 1 cm. and dropped another gold seed, so that the entire tumor-bearing area was infiltrated by the radioactive gold seeds.

The patient made an uneventful convalescence, and is now well six years after operation. This case represents proved carcinoma of the head of the pancreas with no evidence of recurrence at this time.

(Slide) This is the dog's pancreas, running from the tail through the body to the uncinate process. We use colloidal gold, after the work of Flocks and others, and inject it directly into the pancreas. I think you can see the gold here in the black area, as well as the marked reaction and thickening in the tail of the pancreas.

(Slide) This section was merely placed on ordinary x-ray films and allowed to take its own picture. I think you can see the tremendous concentration of the radioactive gold in this region, as well as along the lymphatics, here.

We were able to do this without any evidence of pancreatitis, without any loss of the gold outside the body, and we felt (as shown by others) that a dosage of 1 mc. per gram of tissue would give us about 75,000 rem, which is a fairly high tumorcidal dose.

I have two questions I should like to ask Dr. Harper. First, did the patient get pancreatitis? Second, did he have any trouble with fistulae?

DR. P. V. HARPER JR., Chicago: I want to express my gratitude to Dr. Ireton for his remarks and congratulate him on his spectacular result in his one case.

In answer to both his questions: No, we have had no fistulae and no pancreatitis whatever, much to our surprise.

I would like to emphasize two points. This approach circumvents two objections to the use of conventional radiation techniques, i. e., with radon. The surgeon is not committed ahead of time to procuring radiation sources and having them available, which is necessary if he is going to use radon. This tubing can be kept sterile in the operating room at all times.

The second point is that there is no irradiation going on in the operating room in the implant, so there is no radiation exposure at the time of surgery, as is necessary when one uses conventional radiation techniques. The procedure, therefore, has these two advantages.

When the procedure is terminated, the ends of the tubing, both of which come out through the wound, are sealed and allowed to retract beneath the skin. They cause no trouble. The tubing is left in permanently.

If at any time prior to this it becomes necessary to remove the isotope, if the patient dies and there is an autopsy, or if the patient gets sick and has to have a reexploration, the isotope can be removed.

Experimental Increase of Lung Metastases After Operative Trauma (Amputation of Limb with Tumor)

MALCOLM R. LEWIS, M.D., and WARREN H. COLE, M.D., Chicago

The primary interest of the surgeon in the treatment of cancer should be directed toward eradication of the primary tumor, but the control of metastases is obviously of vital importance, and in fact part of the fight to obtain a cure. Up to date much splendid work has been carried out on dissemination of cancer by the lymphatics and by contiguity. However, dissemination by implantation and by the venous system has been neglected. In our opinion there is need for an intense study of dissemination by these latter two mechanisms. A few years ago we became interested in the question as to what effect operation itself had on the growth of tumor, particularly in regard to metastases. The experiments reported herein were designed to answer this question.

Venous metastases are of unquestioned importance because they are usually the cause of death, except in a few tumors (e. g., those of the oral cavity and neck), where local pressure, malnutrition, and ulceration are lethal factors. Metastasis via the blood stream is dependent upon the transportation of cancer cells from the primary tumor to distant organs. Actually, during the past 50 years there have been several reports in the literature indicating that cancer cells were found in the blood stream, but little attention was paid to these reports, perhaps because identification of cells appeared doubtful. Five years ago one of us (W. H. C.) and associates [1] reported finding cancer cells in the venous blood draining tumors in the rectum and colon. It would be of extreme importance to know whether or not those cells found in the vascular system are viable and capable of forming metastases. In animals there is evidence that only a small portion survives. In experiments, conducted by Zeidman and associates,[2] with sarcoma 241 in mice they found there might be no more than one take for 10,000 cells; yet in our experience with the Walker 256 rat carcinosarcoma 1000 cells might result in as many as 100 metastases. These experiments in animals cannot be construed as being valid for the human being, because they are dealing with homologous cells, not autogenous cells.

In recent clinical experiments conducted by Roberts and associates [3] and Moore and associates,[4] it appears that cancer cells are often found in the venous system of patients with cancer, but usually only in patients with advanced cancer. Yet cells may be found in the venous system in as many as 15% of patients with resectable and potentially curable cancer.[3]

One would suspect that in many patients the virulence of the tumor cells is so low, or the resistance of the host is so high, that loose cells floating in the blood stream may not be viable. If the ratio of virulence of tumor and resistance of the host should be reversed (for one reason or another, e. g., hormonal), then the opposite would be true, and the majority of cells might live. Another important question is whether the

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From the Department of Surgery, University of Illinois College of Medicine.

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patient might be able to kill a small number of cells, but not a large number. Numerous authors, including investigators[5] from our own laboratory, have noted that an increased number of cells results in a higher incidence of takes in animals. In this respect cancer cells behave like bacteria, a small number of which may be killed by the host, whereas a large number may result in an infection. All of these data are related to the question whether an operation (with or without removal of the primary tumor) will influence the growth of the metastases. Most important of all may be the possible ill effect which the operation (through its stress reaction) may have on the resistance of the patient to his own cancer cells.

Methods

An anaplastic mouse tumor (T241) was used. This is a pleomorphic-cell sarcoma which metastasized to the lungs and was originally induced in the subcutaneous tissue of C57BL/6 mice. In our experiments we used mice of this strain between 7 and 9 weeks of age. A sterile suspension of tumor cells was made by finely mincing viable donor tumor in isotonic saline and passing through an 80-mesh steel filter. The cells were counted in a hemocytometer and diluted to 100,000 cells per 0.05 cc.

All mice were aseptically inoculated subcutaneously on the dorsum of the hindfoot with 100,000 cells, using a tuberculin syringe and a 27-gauge needle. The cell suspension was not permitted to age more than two hours. Three per cent iodine solution was used as an antiseptic throughout the experiment. In some preliminary scout experiments we found that cells began to metastasize between the 10th and the 14th day after inoculation. We made this deduction because amputation before this date resulted in cure of nearly all animals. By the time the operation was performed, on the 22d day, the tumors had grown moderately large, usually extending to the ankles (Fig. 1). The experimental animals were anesthetized in an ether jar and the hair clipped from the thigh. A tightened rubber band was slipped over the tumor and onto the thigh to act as a tourniquet (Fig. 2). The extremity was then amputated with scissors above the knee; the stump was not closed, but the skin flaps were approximated and remained so throughout the observation period. The act of slipping the rubber band over the tumor resulted in only mild trauma to the tumor and was not considered a rough manipulation. An equal number of inoculated mice not having an amputation were used as controls. These control animals were taken from the same shipment as the experimental group.

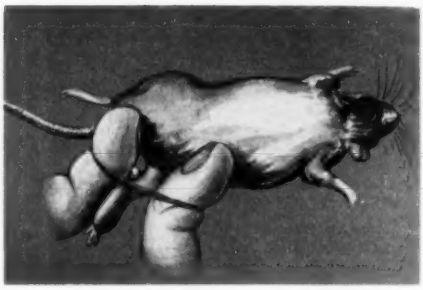

Fig. 2.—Technique of placing rubber band tourniquet on thigh without trauma to tumor.

Animals of both the control and the experimental group were then left to die of their tumors. At autopsy the lungs were removed and examined for metastatic involvement. Those animals having amputations which did not develop metastases, and which therefore continued to live, were killed at 90 days and autopsied. Ten consecutive animals were selected in which visible metastatic deposits were noted to be present. Microscopic examination confirmed the gross diagnosis in all cases, as illustrated in Figure 3.

Fig. 1.—Mouse with tumor of left hindfoot 22 days after inoculation.

Results

The results of the study on incidence of pulmonary metastases in 246 animals is represented in Table 1. In the group having amputation of the tumor-bearing extremity on the 10th day after inoculation, only 7% had pulmonary metastases at death, whereas 36% of the controls had metastases. In this group operation did not increase the inci-

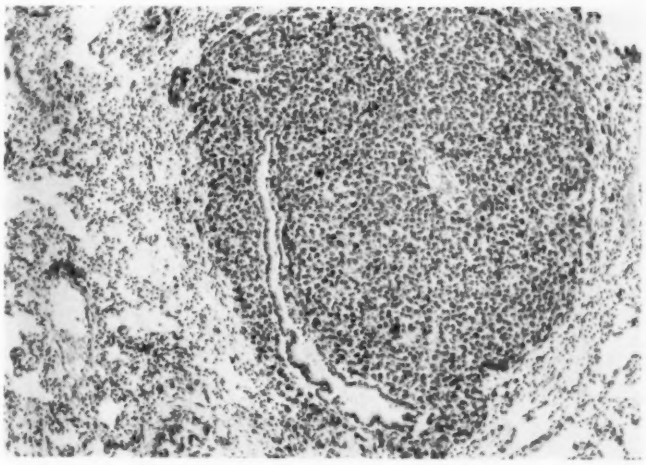

Fig. 3.—Photomicrograph, taken at autopsy, of metastatic nodule in lung of mouse operated on 22 days after inoculation.

TABLE 1.—*Percentage of Pulmonary Metastases in Control Animals and in Those Having Amputation at Varying Periods of Time After Inoculation of Cells*

Day of operation	10th	14th	18th	22d
Control mice with metastases, %	36	44	48	57 (56 mice)
Mice operated on with metastases, %	7	69	71	96 (68 mice)

dence of metastases, presumably because comparatively few cells had desquamated from the tumor at that early date. However, in the other groups the situation was reversed. Operation on the 14th day resulted in a higher incidence of metastases than in the controls, i. e., 69% versus 44%. A similar difference is noted at 18 days. In the group having amputation on the 22d day the greatest difference is seen; pulmonary metastases were observed in 57% of 56 control animals and in 96% of the 68 animals having amputation of the limb bearing the tumor; this difference easily meets the requirements of statistical significance (P is much less than 0.001).

Not only did the animals without amputation develop pulmonary metastases less frequently, but those having metastases had them in much smaller numbers than did the animals operated on (Fig. 4).

The length of life following tumor inoculation can be seen in Table 2. For this computation only those experimental animals dying of tumor were used. Those mice which were cured by the operation and had to be killed for autopsy were not included. Even so, it can be seen that, in all groups, the animals having amputation lived longer.

Comment

In the animal groups herein studied, there can be no doubt that an association exists between operation and the appearance of distant metastases in three out of four groups. The smaller percentage of pulmonary metastases in the mice having amputation of their tumor on the 10th day is readily explainable by the fact that at that early date cells had desquamated from the primary tumor in only a small percentage of animals. However, as the time between inoculation and operation increased, there was an increased tendency for the operation to result in a greater incidence of metastases. We have included the largest number of animals in the 22-day series, because by this time desquamation of cells from the primary tumor must have taken place in the majority of animals; our experiments prove this but do not explain why there were fewer metastases in the control group. There appears to be only one logical explanation of the smaller num-

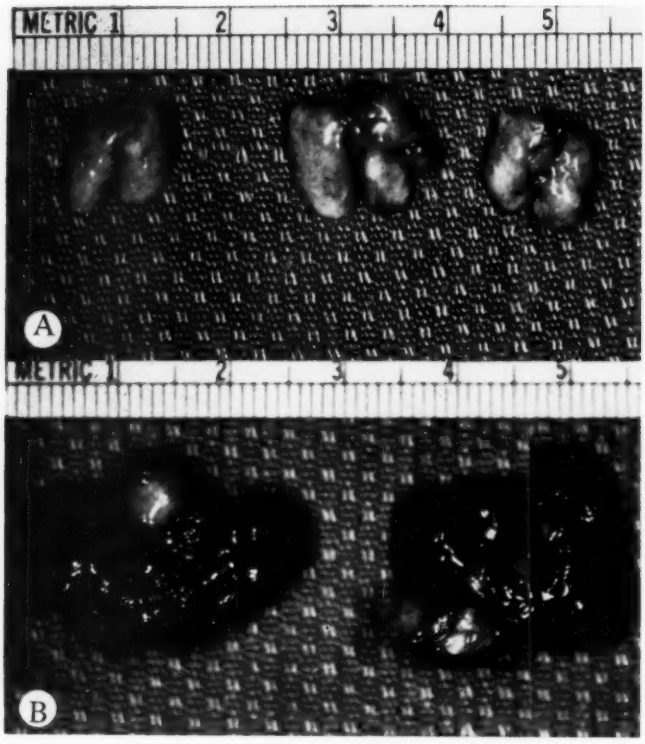

Fig. 4.—*A*, lungs of control animals at time of death. Note single nodular metastasis in center of lung.

B, lungs at time of death, of animals operated on. A small portion of uninvolved lung is noted in each specimen.

TABLE 2.—*Duration of Life of Control Animals and Mice Having Amputation*

Day of amputation		10th	14th	18th	22d
Duration of life, Days	Control mice *	20	28	30	34
	Mice with amputation	37	39	40	45

* These mice, 10 to 56 in number, were taken from the same shipment as the amputated group and after inoculation were kept as controls for each group of mice having amputation. The duration of life in the control and the amputated group will naturally be progressively longer as the days of amputation increase, because the animals dying before the respective dates (10th day, 14th day, etc.) are necessarily excluded.

ber of metastases in the control group: The cells should have desquamated to the lung in an incidence equal to the number in the amputated series, but they must have been killed by the host. This difference becomes more emphatic when we realize that in the amputated series the source of the cells was removed, whereas it was left undisturbed in the control series and should have been capable of desquamation of cells until the death of the animal.

At first glance, it may appear that the increased metastatic rate in the animals operated on is due to the introduction of tumor cells into the blood during the operation. However, it should be recalled that there was minimal trauma incident to the amputation. A rubber band tourniquet was placed on the thigh above the tumor to prevent squeezing cells into the blood stream by the operative manipulation. It is more plausible to believe that the stress of operation (i. e., amputation) lowers the resistance of the animal to growth of the desquamated cells, so that many of the cells lodging in the lung grow into metastases instead of being killed by the host, as they presumably must be in the control animals.

It might be expected that the mice operated on, with their greater volume and in-

cidence of pulmonary metastases, would die sooner than the controls. However, as noted in Table 2, the animals having amputations lived considerably longer. This phenomenon might be explained by an impairment of host nutrition by the tumor, as described by Greenstein[6]: a growing neoplasm continues to provide itself with the nutritive elements necessary for growth regardless of the intake of the host. The host may even develop a state of negative nitrogen balance, while the tumor continues to grow. In the present case, the young mice undergoing amputation were freed of their bulky primary tumors on the 22d day and were able to utilize their food intake for themselves until the pulmonary tumors reached significant size. The control animals, on the other hand, carried a large, growing primary tumor throughout the course of the experiment, and therefore perhaps suffered serious nutritional impairment at an earlier date.

In recent preliminary experiments carried out by Buinauskas and associates in our laboratory, rats were subjected to the stress of a celiotomy (after which the wound was left open for one hour), and an injection of 25,000 tumor cells (aged 12 hours) was made subcutaneously at a distant site. The same number of cells was injected subcutaneously into control rats (of the same shipment) not having an operation. The number of takes was 85% in the operative series and 56% in the control series.

In other preliminary experiments by Chan and McDonald, of this laboratory, rats were subjected to chronic liver damage by feeding carbon tetrachloride for three days. These animals were injected with a suspension of 25,000 cells (aged 12 hours) into a branch of the portal vein. The same number of cells were injected into a branch of the portal vein in an equal number of control animals not treated with carbon tetrachloride. Takes were observed in 64% of the rats receiving carbon tetrachloride, as compared with 21% of the control rats.

In all three of the experiments described herein, an increased number of takes was noted in the "stressed" animals. Each experiment compares the incidence of metastases (pulmonary) or the incidence of takes as influenced by the three different types of stress. In the last experiment (Chan and McDonald) the stress is of a different type in that the control and experimental groups each had a celiotomy prior to injection of cancer cells but in the experimental group liver damage had been produced by carbon tetrachloride. In fact, this liver damage was the only difference between the control and the experimental group. It is difficult to answer the question whether the liver damage acted as stress or whether the hepatic damage in itself allowed a greater incidence of "takes" to develop.

Summary

When 100,000 T241 cancer cells were injected into the hindfoot of mice and the extremity amputated 14 to 22 days later, the incidence of pulmonary metastases was much greater than that in animals similarly inoculated but not having amputation of the limb bearing the tumor. The greatest difference was noted in the group of mice having their amputation on the 22d day: pulmonary metastases were observed in 57% of 56 control animals and in 96% of 68 animals having amputation of the tumor-bearing extremity. It is our belief that the stress of the operation decreases the resistance of the host to the cancer cells being desquamated from the tumor. It must be assumed that cells desquamate from the tumor in the limb with the same frequency in the control group as in the experimental group. Therefore the most logical explanation of the smaller incidence of metastases in the control group must be contained in the assumption that many cancer cells desquamated to the lung in the group without operation are killed by the host resistance, and that this resistance is lowered by the operation in the experimental group.

However, the animals having their tumor-bearing limb amputated lived longer than the controls. This might be explained by the fact that large tumors create malnutrition in the host, because nitrogen is being utilized by the large tumor at the expense of the animal's body.

1853 W. Polk St.

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An Experimental Prototype of Human Colon Tumors

JOSEPH G. FORTNER, M.D., New York

One tantalizing mystery about the pathogenesis of large-bowel neoplasms is that, while common in man, these tumors have rarely been observed to arise spontaneously in laboratory animals. Moreover, the induction of colon tumors by known experimental means has been accomplished infrequently.[1] At the present time, the data of these few successful experiments do not seem applicable to human material.

It was, therefore, with considerable interest that some two years ago we first observed, previously unrecorded, adenomatous polyps and adenocarcinomas of the large intestine in the Syrian hamster.[2,3] Our interest was further heightened by the similarity of these hamster tumors to comparable human tumors and by the great frequency with which they were observed.

Materials and Methods

The experiment was initiated during the period of December, 1954, to April, 1955. Six hundred twenty weanling Syrian hamsters were obtained from a commercial dealer and, after stabilization in the laboratory, were separated into various experimental groups. The diet consisted of Purina Laboratory Chow and water. Their general condition was evaluated daily, and the animals allowed to live out their life span. At the animal's death, complete necropsy and microscopic study were carried out. The details of the experimental testing seem unimportant to the currently reported observations, and are therefore not presented at this time. The tumors are of apparent spontaneous origin, for they occurred in control animals, as well as in test animals.

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Read at the 15th Annual Assembly of the Central Surgical Association, Columbus, Ohio, Feb. 22, 1958.

These studies were supported by grants from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

Drs. Stephen S. Sternberg and Arthur C. Allen were of help in the pathologic studies carried out. Miss Alice W. Gale gave technical assistance.

From the Department of Surgery and the Andre and Bella Meyer Laboratory, Division of Experimental Surgery, Memorial Center for Cancer and Allied Diseases.

Results

One hundred fifty animals died early in the experiment or were unsuitable for study. Of the 470 animals surviving eight months or longer, 52% were found to have tumors. Forty per cent of the tumor-bearing animals had neoplasms of the large intestine. The mean period for development of these tumors was 24 months, with a variation from 10 to 33 months on the experiment. Male animals were found to have colon neoplasms more often than female.

Four types of tumors originated in the large intestine: adenomatous polyps, in 81 animals; adenocarcinomas, in 21 animals; leiomyosarcomas, in 2 animals, and an angiosarcoma, in 1 animal (Figs. 1 and 2). The tumors were found throughout the large intestine, but most commonly in the proximal colon. The cecum was the second area most commonly involved.

Polyps were both sessile and pedunculated. Microscopically their appearance varied from that of a typical adenomatous polyp with benign, mucus-secreting epithe-

Fig. 1.—A segment of colon showing multiple adenomatous polyps.

Fig. 2.—Cecum of a hamster showing a large adenomatous polyp. The surface was found to be involved by carcinoma on microscopic study.

lium to that of carcinoma originating in a polyp (Fig. 3). Adenocarcinomas were found to originate also without evidence of preexisting polyps. About one-third of colon carcinomas were found to have lymph node metastases. One of the leiomyosarcomas of the colon had diffuse abdominal metastatic disease.

Of these large bowel tumors, 10% were associated with a neoplasm of the small intestine or hindstomach, 32% were associated with adrenal cortical hyperplasia, adenomas, or carcinomas. Eighteen per cent of colon tumors in females were associated with ovarian or uterine tumors.

Comment

These studies have revealed a new phenomenon in neoplasia which is of potential importance in delineating the pathogenesis of cancer in man.[3] It is by such study of various phenomena related to the pathogenesis of large-bowel neoplasms that great strides have been made already in the treatment and prevention of this disease in man. Thus, the demonstration that patients with ulcerative colitis are prone to develop colon neoplasms, that many adenomatous polyps

Fig. 3.—Adenocarcinoma of colon showing muscular invasion.

Hamster Tumors

	No. of Tumors
Endocrine organ	
Adrenal	121
Ovarian	8
Islet cell	7
Parathyroid	2
Hormone-susceptible tissues	
Liver	20
Lymphoid	19
Hemangioma of spleen	13
Uterus	9
Thyroid	5
Kidney	3
Glandular tissues	
G. I. tract	124
Cowper's gland	17
Pancreatic	4
Lung (bronchiolar adenocarcinoma)	3

will become adenocarcinomas, and that in many instances these polyps occur in families are a few examples of the practical clinical application of basic studies on the pathogenesis of large-bowel neoplasms. It is hoped that study of the etiology and pathogenesis of the hamster tumors will give further insight into the problem.

As yet, we do not know the etiologic factors for the hamster tumors. However, evaluation of the experimental data suggests that the large-bowel neoplasms in the hamsters are but part of a neoplastic process which selectively involves tissues of glandular type, of endocrine organs or of those organs previously demonstrated to be susceptible to hormone-induced neoplasia (Table). Two tumor types are possible exceptions to this generalization, namely, a squamous-cell carcinoma of the forestomach and malignant melanomas (10).[4] The latter, especially, point up the specificity of the spontaneous tumorigenic process, for nine of the melanomas arose in the skin but no squamous-cell carcinoma of the skin was found. Only 1 of the 470 animals had a squamous-cell carcinoma, and this was of the forestomach.

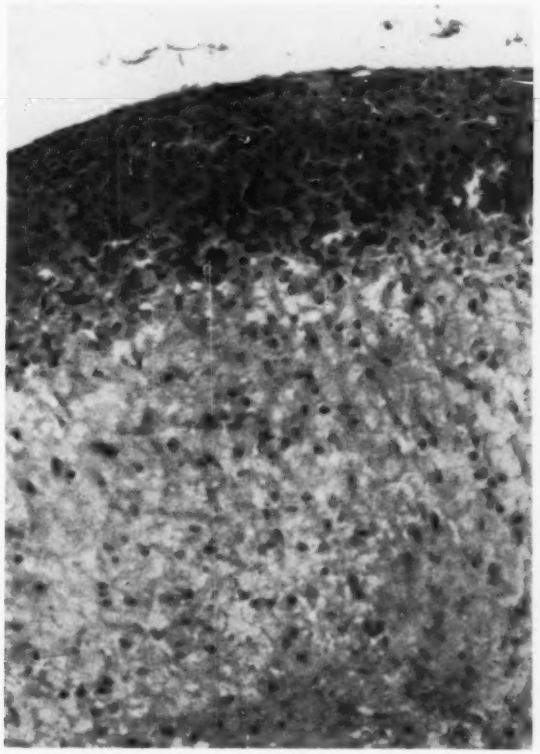


Fig. 4.—Adrenal cortex showing destruction of the zona reticularis and zona fasciculata. The zona glomerulosa is intact.

Figure 5

Fig. 5.—Bisected adrenal cortical carcinoma is shown on the left of the bisected kidney.

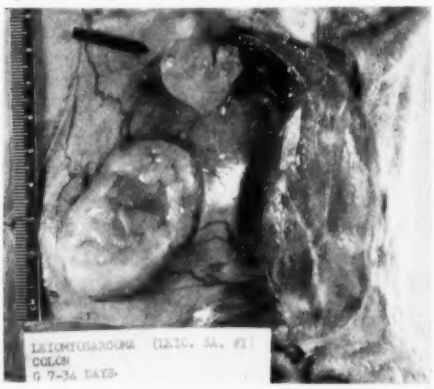
Figure 6

Fig. 6.—Appearance of a subcutaneously transplanted adenocarcinoma originating in the pancreas of a hamster. The arrow points to an axillary lymph node metastasis. Tumor implanted for 24 days.

It seems likely that the neoplasms have an etiology which is common to all. In addition to the previous considerations, the various tumor types had a similar latent period for development and occurred under similar conditions. The association with, and predominance of, tumors and pathologic lesions in the adrenogenital system suggests that a hormonal imbalance[5] may be the basic causal mechanism for the tumors observed in these animals. With rare exception, the animals had marked pathologic alterations of the zona fasciculata and zona reticularis of the adrenal cortex (Fig. 4). In addition, nearly 50% of the tumor-bearing animals had carcinomas (Fig. 5), adenomas, or marked hyperplasia of the adrenal cortex. Ovarian tumors, as well as cystic changes in the ovaries and ovarian luteinization, were seen. Evidence of estro-

Fig. 7.—Appearance of a subcutaneously transplanted adenocarcinoma originating in the small intestine of a hamster. Tumor implanted for 10 days.

Fig. 8.—Appearance of a subcutaneously transplanted leiomyosarcoma of the colon originating in a hamster. Arrow points to a large axillary lymph node metastasis. Tumor implanted for 34 days.



gen stimulation of the vagina and uterus was also commonly observed. Testicular atrophy was nearly uniformly present in animals 9 months of age or older. These various findings seem clearly to indicate the presence of a hormonal imbalance. The pathologic alterations commonly seen in the liver and kidneys would seemingly potentiate any such hormonal imbalance.

As a direct outgrowth of the studies herein briefly described, we have established in active transplant form 25 different tumors. In this spectrum of spontaneous, transplantable hamster tumors are a pancreatic adenocarcinoma (Fig. 6), a small intestinal adenocarcinoma (Fig. 7), and a leiomyosarcoma of the colon (Fig. 8). Tumor implants grow in 100% of animals, metastasize, and no additive measures, such as use of cortisone or x-rays, are needed. investigators.

Conclusions

Adenomatous polyps, adenocarcinomas, leiomyosarcomas, and an angiosarcoma of the large intestine have been observed to arise spontaneously in 40% of tumor-bearing Syrian hamsters. These form 25% of the total animals of the experiment. The tumors are grossly and microscopically very similar to human tumors of comparable types.

The neoplasms of the large bowel are but part of a phenomenon of generalized neoplasia which selectively involves tissues of glandular types, of endocrine organs, or of organs previously demonstrated to be susceptible to hormone-induced neoplasia. It is believed that this neoplastic phenomenon may be the result of a hormonal imbalance.

Transplantable, spontaneous adenocarcinomas originating in the pancreas and small intestine and leiomyosarcoma of the colon are growing in active transplant form and are available to interested investigators.

Memorial Center for Cancer and Allied Diseases, 444 E. 68th St.

Addendum

Tumor incidence and related data will be revised in a subsequent publication. Animals incompletely studied at the time of preparation of this manuscript have been considered as negative in calculating the data for this paper. Subsequently, many of these animals have been found to have tumors of the types described herein.

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DISCUSSION

ON PAPERS BY DRS. LEWIS, MCDONALD, AND COLE AND DR. FORTNER.

DR. JOHN M. WALKER, New York: I want to congratulate both Dr. Lewis and Dr. Fortner. I think Dr. Lewis has brought up a very important subject—and that is why and when we get "takes" of cancer cells. At the Memorial Hospital we have found a very high incidence of cancer cells by smears taken routinely from the cul-de-sac of patients with carcinoma of the bowel and rectum. These cells are present at the time of operation, and the smears are taken before any procedure is done. The figures are so high for these carcinoma cells in the peritoneum that it scares you, and you wonder why you ever get a cure of cancer. The answer must be that the host has a good resistance to it. This is the only answer we can come up with now.

I think Dr. Fortner should be given a vote of thanks by everybody. This work is most significant. It gives the clinician and the investigator another inexpensive strain of animals in which to study cancer.

These tumors that you have seen appear similar to human tumors. The high incidence of tumors in an animal with such a short life span, and the ease of transplant of many of the cancers, make the hamster an excellent subject for cancer investigation.

This should be of interest not only to the surgeon but to those in related fields—biology, genetics, immunology, and endocrinology. I am sure it would be of interest to this group to know how Dr. Fortner stumbled on this strain.

When he was a resident, he had his gallbladder removed, and he became interested in the gallbladder and bile and the liver. Then he began to think that maybe these people who have carcinoma of the gallbladder have something in their bile—a carcinogenic agent—that causes it; so he collected bile all over New York City. Almost everyone in the city who had a carcinoma of the gallbladder was under his watchful eye, and he would say to the doctor: "If you have a T-tube in, will you save the bile for me?" He collected bile by the gallon, and then he started his experiments.

As so often happens, when one starts an experiment, one often goes off in a different direction. Dr. Fortner found out that when he injected the hamsters and ran controls on them, the controls also developed cancer. Then he began studying these animals, and he is still in the process of trying to evaluate whether the carcinogenic agent given by injection of human bile plays any part, or whether these animals all develop carcinoma spontaneously.

I would like to congratulate Dr. Fortner on being willing to stick his neck out by implying that the majority of tumors he has found are related to hormonal changes. This should lead to further study of the endocrine glands, especially their influence on cancer of the gastrointestinal tract.

The simple question of why polyps occur is a good illustration. There has been relatively little work done on this important subject, as compared with the studies that have been carried out on breast, prostate, and gynecological cancer in their relation to various hormones. Perhaps Dr. Fortner will be good enough to come back in four years and give us the answer to this problem.

Dr. Warren H. Cole, Chicago: When we reviewed Dr. Lewis' data, trying to explain them, we thought first that the amputation had dislodged cancer cells from the tumor in the extremity, and that they had gone to the lung, thus explaining the increased number of metastases in the amputation group. However, continued study of this possibility led us to the conclusion that the trauma which Dr. Lewis had inflicted on the tumor was minimal, and we then concluded that the increased number of metastases must be due to operative stress.

Along about that same time Dr. Peter Buinauskas was conducting a similar experiment in which celiotomy was performed in a group of rats, and 10,000 cells were injected subcutaneously at a distance from the site of the celiotomy. We found that the takes in control animals not having celiotomy were only half as many as in animals having celiotomy; here we have nothing but the operative stress to explain the difference. That is an added reason for our thinking that in Dr. Lewis' experiments the difference must be explained on the basis of operative stress.

Going still further, Dr. Chan, also working in our laboratory, tried the effect of a chemical (carbon tetrachloride) on the take of cancer cells when it was injected into the portal vein. He gave rats carbon tetrachloride for three consecutive days, which, as you know, inflicts fairly severe damage on the liver. Then he injected 10,000 Walker 256 cells into the portal vein. A similar number of animals serving as controls were inoculated with an equal number of cells, but were not given carbon tetrachloride. Much to our surprise, the takes in the animals having the carbon tetrachloride were twice as high as in the controls.

Was it the chemical stress that produced this, or was it the damage to the liver? We do not know. Perhaps it is both.

The big question is whether this work applies to human beings. I am convinced that in animals certain kinds of stress will increase the number of "takes" when they are inoculated with cancer cells. But does it apply to human beings? I am afraid it does.

That is not bad news at all. It is good news, for we already know that surgery is the best agent we have in treating cancer; if a decrease in resistance to cancer cells is induced by stress, I think we have a pretty good chance of neutralizing that reaction.

First, we have to find out exactly what it is. Is it an alarm reaction? We can get information on that point by giving corticotropin and cortisone to these animals. If it is alarm reaction, these drugs will do the same thing. If the decreased resistance to tumor cells is produced by the alarm reaction and we neutralize it, what will this neutralization do to the patient's ability to withstand the operation? It might increase the mortality rate. At any rate, this phenomenon has given us something new to think about.

Dr. William D. Holden, Cleveland: I should like to congratulate both Dr. Lewis and Dr. Fortner. These studies are quite remarkable, and a great deal of significance must be attached to both these experiments which have been reported today.

In Dr. Fortner's abstract he mentioned something that he did not have time to comment on in his presentation. I think it would be worth while

if he were given a minute or two to discuss the possible pathogenic relationship of the cytoplasmic inclusion bodies found in human colonic polyps.

These cytoplasmic inclusion bodies were first observed, some three years ago, at Western Reserve by Dr. Leuchtenberger, a cytochemist, in adenomatous polyps of the large intestine. This was an extremely intriguing observation, and since that time these inclusion bodies have been found in every one of literally hundreds of polyps or polypoid carcinomata of the colon. I thought perhaps Dr. Fortner might take a few moments to discuss the possible significance of these observations.

DR. JOSEPH G. FORTNER, New York: In response to Dr. Holden's question: We have examined several of the polypoid lesions and have been unable to find cytoplasmic inclusion bodies ourselves. Dr. Leuchtenberger and I are collaborating in studying this problem further.

Pathologic Aspects of Cardiac Valvular Insufficiencies

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Insufficiency may occur in each of the cardiac valves. Involvement of the pulmonary and tricuspid valves is much less common than involvement of the valves on the left side of the heart. Moreover, pulmonary insufficiency occurs only rarely as a primary disease. It is usually an incidental complication of pulmonary hypertension. Likewise, tricuspid insufficiency does not often occur as an isolated disturbance. It may complicate atrial septal defect, but more frequently is associated with significant rheumatic disease of the aortic and mitral valves. For these reasons I shall discuss only aortic and mitral insufficiency.

Incompetence at the Aortic Valve

The diastolic pressure of the systemic arterial system depends on (1) the volume of systemic flow in a given time, (2) the resistance to flow, and (3) the competence of the aortic valve. All other factors being equal, if the peripheral resistance is low, the diastolic pressure is low. Likewise, if the other factors remain constant and if aortic insufficiency is present, the diastolic pressure is low. Usually when aortic insufficiency is present, the low diastolic pressure is a result of a combination of the valvular incompetence and low peripheral resistance.

In the presence of a competent aortic valve, conditions which cause chronically low peripheral resistance include patent ductus arteriosus, systemic arteriovenous fistula, some instances of Paget's disease of bone, and thyrotoxicosis.

In this communication we are concerned principally with those conditions of the aortic valve and certain lesions in structures closely related to the aortic valve that are responsible for failure of maintenance of normal diastolic pressure.

The Normal Valve.—In order to appreciate best the basis for incompetence of the aortic valve, it is appropriate to review certain aspects of the structure of the normal aortic valve.

The three aortic cusps, the right, the left, and the posterior, may be looked on as three independent units, each connected to its respective segment of the aortic wall (Fig. 1). It is important to recognize that each aortic cusp has two lateral attachments

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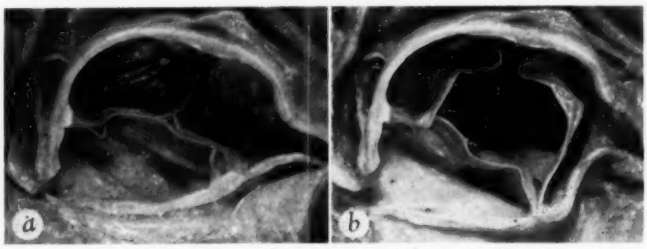


Fig. 1.—Features of the normal aortic valve. In each case the specimen of intact aortic valve is viewed from above.

(*a*) The closed valve. Each leaflet is longer than a straight line between its two lateral attachments, creating redundancy. This allows normal contact of the three leaflets at the central point of the aortic orifice. (*b*) Valve partially open. The valve leaflets balloon freely toward the lateral wall of the aorta during ventricular systole.

to the aortic wall and an inferior attachment to the root of the aorta.

Between the attachment of one lateral extremity of a cusp to the aortic wall and that of the other extremity the tissue is greater than it would be if the cusp followed a straight line between these two attachments. There is, in the normal cusp, an excessive amount of tissue. This allows the central part of each cusp to extend to the center of the aortic orifice. At this point, the centers of each of the three leaflets touch during closure of the valve. Radiating from this central point of the aortic orifice are the contacts of halves of each cusp with the adjacent halves of their neighbors. The space, or potential space, between the lateral attachments of two adjacent cusps at the aortic wall is referred to as a commissure. In the normal aortic valve, three such junctional zones or commissures exist (Fig. 1*a*).

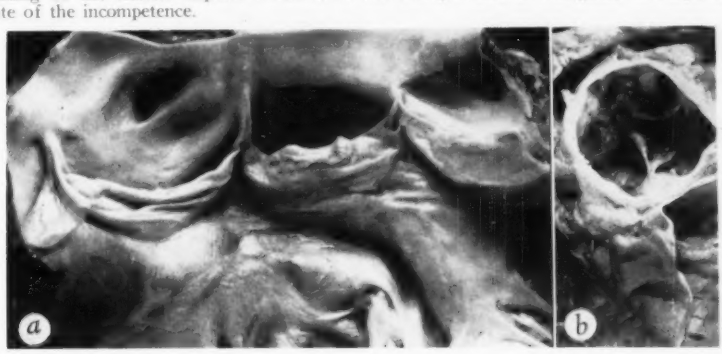
In the normal aortic cusp, there is a margin of safety with regard to the length of the cusp. Thus the cusp is longer in its superoinferior dimension than is necessary for contact with its fellow cusps. This concept is supported by the fact that the cusps do not touch each other just at their free edges; rather, the area of contact extends downward for a distance of several millimeters from the upper edge. The lowermost margin of contact is spoken of as the "line of contact."

Should the orifice dilate, within limits, the extra tissue between the line of contact and the free edge of the cusp may prevent aortic insufficiency. Likewise, in the process of shortening of the leaflets due to intrinsic disease, the extra tissue represents a certain margin of safety between competence and incompetence of the aortic valve.

Rheumatic Aortic Insufficiency.—Classically the aortic insufficiency which results from rheumatic carditis is manifested by intrinsic disease of the valve leaflets. Grossly it consists of thickening and, more important, shortening of the cusps. In the opened specimen of the heart affected by rheumatic aortic insufficiency, the shortening of the aortic valvular leaflets may be appreciated only when comparison is made with a normal heart by use of the same perspective. In the heart in which aortic insufficiency is present, one may see more of the aortic sinuses than is possible in the normal heart. The shortening of the cusps is most marked in their central portions and least at their lateral, or commissural extremities (Fig. 2*a*). Because of this fact, the insufficiency in the functioning valve is represented by a triangular defect at the center of the aortic orifice (Figs. 2*b* and 3).

Fig. 2.—Rheumatic aortic insufficiency. (*a*) The open valve. Thickening and, particularly, shortening of the leaflets are evident. This view makes it possible to see readily into the depths of the sinuses.

(*b*) Valve in the unopened state and viewed from above during ventricular diastole. The shortening of the leaflets imparts a defect to the valve, which is triangular in shape and is the site of the incompetence.



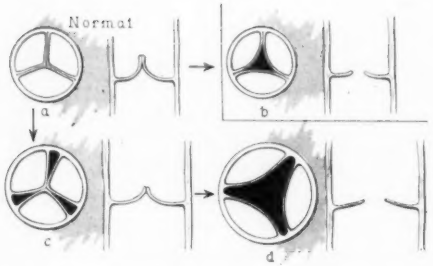


Fig. 3.—Diagrammatic representations of the aortic valve as viewed from above and on longitudinal sections.

(*a*) The nature of the normal cusps is brought out, showing that the redundant character of the cusps allows the three to join in the central point of the aortic orifice. The longitudinal section indicates a certain margin of safety in the length of the normal aortic cusps, wherein contact is made over a relatively large area. Shortening of the cusps or deviation of one from the other, up to a point, will still be associated with competence of the valve.

(*b*) In rheumatic aortic insufficiency the intrinsic lesion is shortening of the leaflets, which causes a triangular defect in the center of the aortic valve during ventricular diastole. This is the site of the incompetence.

(*c* and *d*) Dilatation of the aorta, as in syphilitic aortitis, is manifested by a separation of one leaflet from the other. In (*c*) a hypothetic state is represented in which separation occurs only at the commissures. In the actual disease the aorta dilates more or less equally throughout its circumference, so that the deficiency in the aortic valve is represented not only by separation at the commissures but also by separation of one leaflet from its other two neighbors, throughout their entire length, not as portrayed in (*c*) but as is shown in (*d*).

At the commissures, the cusps are in contact.

In rheumatic aortic insufficiency, the degree of fusion between two or more adjacent leaflets varies. Minor degrees of fusion do not create significant stenosis. In other cases the amount of fusion between the adjacent leaflets is so great that the significant aortic stenosis is associated with the insufficiency. Further detail concerning the changes when stenosis and insufficiency coexist at the same aortic valve will be discussed later.

Syphilitic Aortic Insufficiency.—The classic gross picture of syphilitic aortitis is that of dilatation of the thoracic aorta (Fig. 4*a*). The insufficiency of the aortic valve that may accompany this change is generally conceded not to be the result of primary valvular disease. Rather, the valvular changes are secondary to the primary ones in the aortic wall.

Since each aortic leaflet can be considered a separate unit, it becomes apparent that as the aorta dilates, each leaflet will be carried away from the other two. Thus the space between the lateral attachments of two adjacent leaflets to the aortic wall increases; this condition usually is referred to as "separation of the aortic valve commissures." While separation at the commissures of the aortic valve is usually given as the essential lesion in aortic valvular insufficiency of syphilitic origin, the process leading to incompetence of the aortic valve is probably more complicated. If one considers, again, the fact that each aortic cusp is a separate unit and attached to a corresponding portion of the aortic wall, then it is apparent that dilatation of the aorta will explain not only the separation at the commissures but also the stretching of the leaflets. As the aorta dilates, the distance between the two lateral attachments of a leaflet increases (Fig. 3). As this happens, the valvular leaflet is stretched, often to its maximal length. With this development, the redundant portion of the valve which normally approaches the center of the aortic orifice is pulled away from the center. This bowing effect on individual cusps causes an increase in space between the valve leaflets not only at the commissures but also at the center of the aortic orifice and along the entire contact aspect of the cusps (Figs. 3*c* and *d* and 4*b*).

Certain intrinsic changes also occur in the cusps of the aortic valve in syphilitic aortitis, but these are probably secondary to the mechanical effects of stretching of the leaflets and the concomitant aortic insufficiency. The so-called rolling of the free edge of the aortic leaflet given as a classic change in syphilitic aortitis is probably caused by the mechanical effects of the regurgitant stream. This process adds an element of shortening to the cusps.

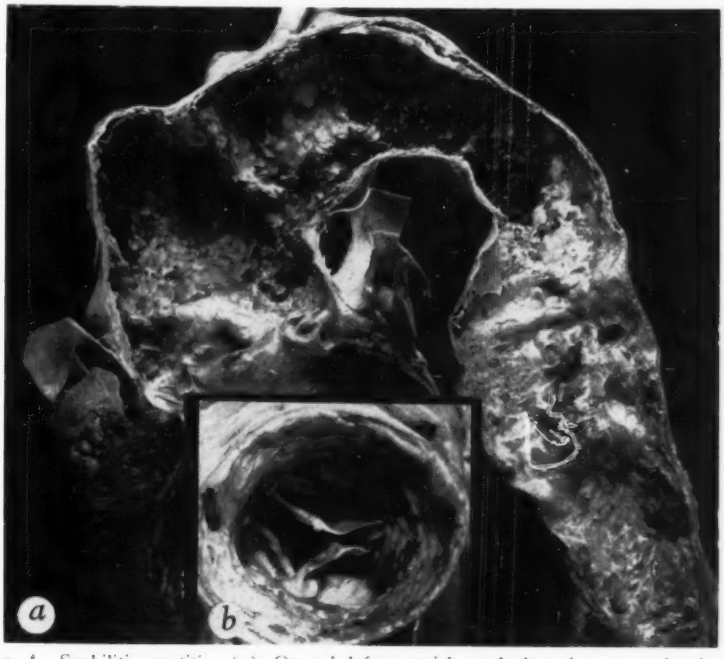


Fig. 4.—Syphilitic aortitis. (*a*) Opened left ventricle and thoracic aorta, showing the classic dilated aorta of syphilitic aortitis. (*b*) Aortic valve viewed from above. The dilatation of the aorta has caused bowing of one leaflet, which has become separated from its two neighbors and is responsible for the aortic insufficiency.

Congenital Bicuspid Aortic Valve.—This type of valve often yields no recognizable symptoms of being incompetent. Rarely, however, in the absence of associated stenosis it may be significantly incompetent. In my experience this tendency seems more prevalent among patients also having coarctation of the aorta than those who do not.

The exact mechanism for the valvular incompetence of the congenital bicuspid aortic valve is not entirely clear. The congenital raphe that occurs in one of the two cusps may be related. This is a ridge of tissue containing aortic medial tissue that extends along the aortic surface of the conjoined leaflet from its free edge to its aortic attachment (Fig. 5). Possibly this tissue interferes with free motion of the leaflet, and it may introduce an element of rigidity, which may set the stage for im-

Fig. 5.—Congenital bicuspid aortic valve. The conjoined leaflet is larger than the other. A raphe extends from the aortic wall from a point between the two coronary ostia onto the aortic face of the conjoined leaflet. Shortening of width of the leaflet, and possibly its greater length as compared with that of its neighbor, were the basis of severe incompetence in the case. (From an adult with coarctation of the aorta.)

proper apposition of the two leaflets. The congenital bicuspid aortic valve may be incompetent simply on the basis of its intrinsic structural nature. At other times the valve may acquire calcific disease, associated with stenosis and varying degrees of incompetence.

Aortic Insufficiency Associated with Aortic Stenosis.—The same degree of aortic stenosis is more serious when aortic insufficiency is associated than when it is not. The barrier to the outflow of blood from the left ventricle by a stenotic valve needs to be measured in terms of the amount of blood that the left ventricle attempts to eliminate in a given period of time. It is obvious that with the same effective forward flow the left ventricle has to eliminate more blood when aortic insufficiency coexists with stenosis than it does when the stenosis is not associated with insufficiency.[1] Thus, in two cases in which stenotic orifices are of the same size and the systemic blood pressures are of the same magnitude, the systolic pressure in the left ventricle will be higher in the case in which insufficiency is coexistent than in the case in which it is not.

In many stenotic aortic valves one of the three commissures is obliterated by fusion of two adjacent cusps, usually the right and left. The resulting fusion of the two leaflets converts the aortic valve into a bicuspid valve (Fig. 6*a* and *b*). One leaflet, the conjoined one, is immobile.[2]

Fusion of the adjacent cusps takes the form of a calcified raphe that joins the aortic wall with the zone of fusion of the two leaflets. The resulting conjoined leaflet is made immobile not only by its intrinsic calcific disease but also because of its rigid fixation to the aortic wall by the calcified acquired raphe. The only chance for the valve to open is motion in the third cusp. In many classic examples of this condition the third leaflet is able, in spite of its intrinsic disease, not only to open a limited amount but also to close completely or nearly so, thereby preventing any significant regurgitation.

At the opposite end of the scale are those cases of aortic valvular stenosis in which adjacent cusps are fused at each of the three commissures (Fig. 6*c*). This fusion may extend for a considerable distance from the aortic wall toward the center of the lumen. Obviously, if the fusion at each commissure extended to the center of the lumen, there would be no aortic orifice. Some opening, however narrow, of course, exists. The preservation of an opening when tricommissural fusion exists depends on the intrinsic shortening of the valvular leaflets. This shortening, coupled with fixation of each leaflet to the others by fusion at the commissures, yields an aortic valve which is no longer a valve in the usual sense. The aortic valve has been converted to a structure which may be compared to that of a metal washer having a central perforation which remains the same size throughout the cardiac cycle. It is obvious that such a valve not only causes obstruction to the outflow of blood from the left ventricle but also allows regurgitation.

The two types of aortic stenosis involving tricuspid aortic valves which have been described represent the two purest forms of this disease. In the first there was fusion at only one commissure, allowing only the third leaflet to function as a valve flap. The possibility for complete closure of the aortic valve during ventricular diastole exists in this type of valve. In some instances, however, the presence of irregularly deposited calcific spurs may prevent the single functioning cusp from closing the orifice; thus some aortic insufficiency may exist. In the second type of aortic stenosis mentioned, fusion at the three commissures eliminates any valvular function.

There are also transitional states between these two types of aortic stenosis in hearts having three aortic cusps. These transitional forms usually consist of fusion at two of the three commissures (Fig. 6*d*). This results in an orifice which has the shape of an exclamation point laid on its side. During ventricular diastole the narrowest part of the orifice is at the commis-

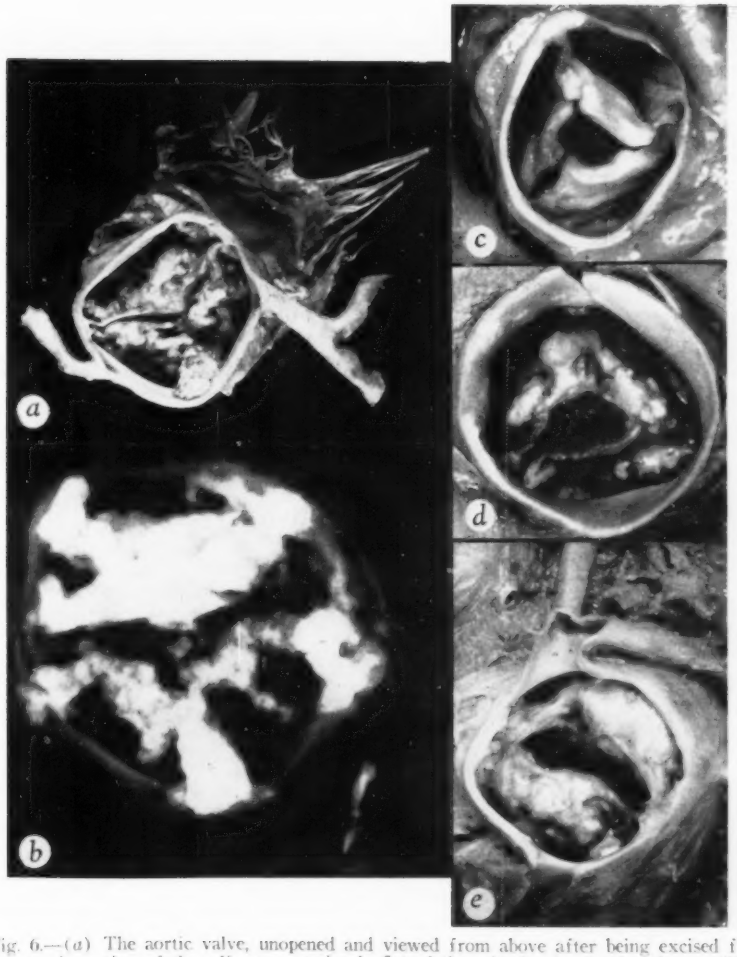


Fig. 6.—(*a*) The aortic valve, unopened and viewed from above after being excised from the heart. A portion of the adjacent anterior leaflet of the mitral valve is also shown. There is a severe degree of calcific aortic stenosis in which the right and left aortic cusps (lower portion of illustration) have become fused by a calcified raphe. These two leaflets are immobile. At the opposite end of the valve is the thickened, but still somewhat flexible, posterior leaflet. Its flexibility depends on its not being adherent to the other two leaflets. Such a valve is stenotic but not incompetent, because the posterior cusp can close the orifice by almost perfect apposition with the conjoined cusps.

(*b*) Roentgenogram of the specimen of calcific aortic stenosis illustrated in (*a*). It shows the severe calcification of the leaflets at the junction of the right and left leaflets, which is the calcified raphe. It is evident from the calcification of the conjoined leaflet and of the union with the calcified raphe that the leaflet is immobile. Only the opposite posterior leaflet can open.

(*c*) Aortic stenosis with tricommissural fusion; aortic valve unopened and viewed from above. Because of fusion of each of the cusps at each commissure, the valve cannot open further than its present state and cannot close beyond its present state. Such a valve orifice represents a fixed structure, and the tissue no longer has a valvular function.

(*d*) Aortic valve with calcific stenosis and insufficiency. There is fusion at two commissures, which, taken with the calcification of the three leaflets, creates a rigid structure in which the only possible change in size of the orifice during the cardiac cycle would exist at the one commissure where fusion has not occurred (left lower portion of illustration). Such a valve, like that illustrated in (*c*), is not only stenotic but also insufficient.

(*e*) Congenital bicuspid aortic valve viewed from above. The valve is severely calcified, and there is fusion of each leaflet with the other at each commissure. This creates a fixed structure in which the orifice did not change with the cardiac cycle, thus yielding a picture of coexistent aortic stenosis and insufficiency.

sure at which fusion is not present, while the widest point of the orifice lies at one of the two fused commissures. In such aortic valves the changes are essentially similar to those in the congenital bicuspid aortic valve when calcification with fusion has developed at one of the two commissures. Here a small amount of tissue on each side of the commissure between the nonfused leaflets tends to approximate during ventricular diastole, while at the other (fused) commissures the orifice is held in an open state throughout the cardiac cycle.

In calcific aortic stenosis complicating congenital bicuspid aortic valves the coexistence of aortic insufficiency is a common phenomenon. In cases in which fusion has taken place at both commissures, the alteration in the valve is essentially the same as that in the tricuspid aortic valve fused at all three commissures. The orifice is held open throughout the cardiac cycle, and, as has already been suggested, the valvular tissue no longer functions as a valve but, rather, represents a fixed and narrow perforation in a membrane across the aortic orifice (Fig. 6*e*).

In some cases of congenital bicuspid aortic valve with stenosis fusion occurs at only one commissure. Beyond the fusion along the line of the commissure, the two leaflets are held apart in an open and fixed state, while at the other commissure, where there is no fusion, varying degrees of mobility may be present, with a tendency toward approximation of the two leaflets at this region during ventricular diastole. However closely these two leaflets may approximate at this point, there is always a persistent opening near the site of fusion.

Congenital "Dome-Shaped" Aortic Stenosis and Insufficiency.—A congenitally bicuspid aortic valve is not usually stenotic unless disease develops. As has already been indicated, such stenosis is usually attended by insufficiency. Stenosis and insufficiency occur as integral manifestations of the congenital malformation in other types of congenitally deformed aortic valves. The simplest of these forms bears close anatomic similarity to the pulmonary valve when it is involved in congenital dome-shaped stenosis. For our purposes this variety of deformity may be called "simple dome stenosis." A somewhat more complicated variety of dome stenosis exists and may be called "unicommissural dome stenosis" of the aortic valve. In the latter, as the name implies, there is only one commissure in the valve.

Such a valve may be viewed as having but one cusp, which is so constructed as to give the orifice the shape of an exclamation mark. The narrow part of the orifice is at the single commissure, while the widest part lies opposite the commissure. The single leaflet may be said to start at the aortic wall at the commissure. It then extends across the orifice without making contact with the aortic wall, bends on itself,

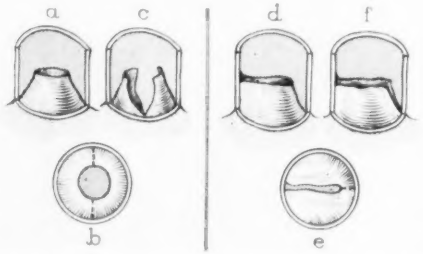


Fig. 7.—Dome-shaped congenital aortic stenosis and insufficiency.

(*a*, *b*, and *c*) Simple dome-shaped stenosis and insufficiency. The intact valve is portrayed in (*a*). In (*b*) the dotted line indicates a plane of section such as would be done in a commissurotomy in which an incision was carried into the valve from each side of the stenotic orifice. The resulting change is represented by (*c*), in which two flaps of valvular tissue not attached laterally to the aortic wall would be created.

(*d*, *e*, and *f*) Unicommissural dome-shaped aortic stenosis and insufficiency. In (*d*) the intact valve is portrayed. In this there is one commissure, and the valvular tissue may be considered simply to be one cusp which is bent on itself and fixed laterally at two sites to the aortic wall to form the single commissure. In (*e*) the dotted line opposite the single commissure represents the section which would be used if valvulotomy were performed. The resulting structural change is represented in (*f*), wherein two flaps of tissue result which are attached laterally to the wall of the aorta at the site of the commissure; opposite it, at the site of the commissurotomy, the two flaps lack lateral attachment to the aortic wall, and so incompetence of the valve results.

and then returns to make a second connection with the aortic wall, and so to create the single commissure (Fig. 7).

In both the simple and the unicommissural variety of dome stenosis raphes extend from the aortic wall onto the aortic face of the deformed leaflet. Although these raphes may be looked on as representing abortive commissures, they do not usually extend very far from the base toward the free edge of the valvular tissue. In this way the raphes constitute inadequate lateral supports for the valvular tissues to the aortic wall.

In both varieties of dome stenosis, it is pertinent to recognize that division of the valve deprives the valvular tissue of proper attachment to the aortic wall. The resulting units become redundant and cause incompetence of the valve.

Marquis and Logan[3] have stressed the great likelihood of complicating aortic insufficiency by valvulotomy on a congenitally stenotic aortic valve. One may wonder why, if the reasoning given is correct, no deleterious effects follow valvulotomy of the pulmonary valve. The answer to this question is that an incised "dome-shaped" pulmonary valve is, in fact, not a competent valve. Fortunately, with regard to the problem of the pulmonary valve, incompetence of the valve does not yield significant insufficiency because the normally low pulmonary arterial pressure is not significantly greater than the right ventricular diastolic pressure.

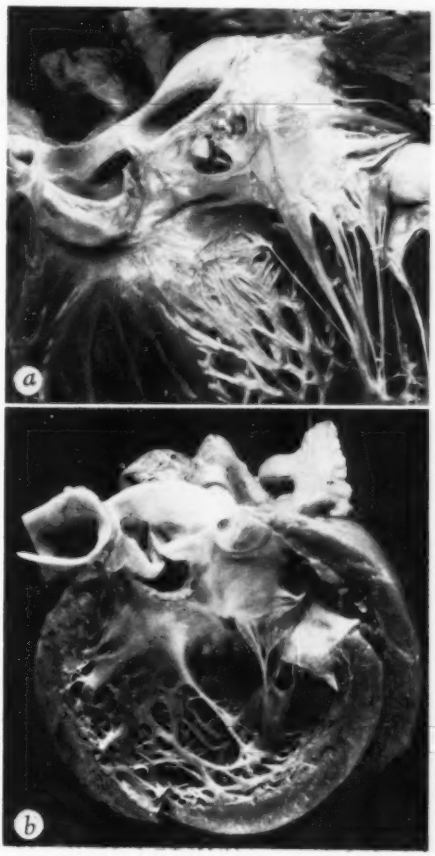
At the aortic valve, in contrast, the large differential in diastolic pressure between the aorta, on the one hand, and the left ventricle, on the other, makes a surgically created valvular insufficiency of great significance.

On theoretical grounds, it appears that if a dome-shaped aortic valve needed to be incised at the site of an absent commissure, the only chance of prevention of aortic insufficiency would be the sewing of each side of the incised valve to the aortic wall, thereby artificially creating a commissure. I realize, however, the inherent difficulties in making a nonstenotic and competent valve by such steps, which represent a challenge to the field of surgery.

Bacterial Endocarditis.—When bacterial endocarditis causes significant destructive changes in the aortic valve, the resulting valvular insufficiency is usually responsible for death during the bacteriologically active phase of the disease.

Fig. 8.—(*a*) Left ventricle and aortic valve in a case of healed bacterial endocarditis involving a congenital bicuspid aortic valve. The posterior of the two cusps has multiple perforations in it, which had made the valve incompetent. Evidence of incompetence is additionally present in the form of regurgitant lesions, appearing as a white network along the surface of the ventricular septum.

(*b*) Left ventricle and aortic valve in a case of ventricular septal defect associated with aortic insufficiency.



In relatively unusual cases in which the bacterial infection is overcome and destructive valvular changes have occurred, the patient survives for some months, or a few years, with chronic aortic insufficiency. The bacterial endocarditis produces erosion or perforations in the aortic cusps (Fig. 8*a*). Preexisting diseases include congenital bicuspid aortic valve, minor degrees of fusion at the commissures resulting from preexisting rheumatic fever, and, uncommonly, calcific aortic stenosis and insufficiency. Although the classic teaching is that bacterial endocarditis almost invariably affects valves previously diseased, in some hearts with bacterial endocarditis it is difficult to demonstrate that prior disease existed.

Uncommon Conditions Causing Aortic Valvular Insufficiency or Functionally Comparable Conditions

Among patients having signs suggestive of incompetence of the aortic valve, there are several relatively uncommon conditions that should be entertained in the differential diagnosis of the commoner varieties of aortic insufficiency. These will now be discussed.

Aortic Insufficiency and Ventricular Septal Defect.—In some instances of congenital ventricular septal defect involving the outflow portion of ventricular septum, aortic insufficiency may coexist. Usually the defect occupies a specific location. From the left ventricular aspect it lies inferior to the adjacent portions of the right and posterior aortic leaflets. The defect as seen from the right ventricular side lies posteroinferior to the crista supraventricularis. Since the defect is bordered by the aortic valve, the aorta fails to have a connection with the ventricular septum at the site of the defect. Deviation of the aorta from its normal relationship with the ventricular septum occurs. With this deviation the portions of the aortic cusps which lie adjacent to the ventricular septal defect prolapse (Fig. 8*b*). These two factors seem to be the essential ones causing aortic insufficiency in association with ventricular septal defect. There are, in addition, fibrous changes in the valvular tissue adjacent to the ventricular septal defect, and with the retraction caused by these changes the insufficiency may be accentuated.

Rupture of an Aneurysm of an Aortic Sinus.—Another condition which may cause run-off of blood in the aorta because of a relationship to the aortic valve is a ruptured aneurysm of an aortic sinus valvula. Most commonly these aneurysms involve the right aortic sinus. When one ruptures, blood is diverted into the outflow tract of the right ventricle. Such aneurysms are not infrequently associated with an immediately subjacent ventricular septal defect. Less common than aneurysms of the right aortic sinus is that involving the posterior (noncoronary) aortic sinus. Rupture of an aneurysm so located usually is into the right atrium, rarely into the right ventricle.

Aneurysms of the left aortic sinus are rare, but when they occur, they may rupture into the pericardial sac and produce either fatal hemopericardium or a false aneurysm of the left aortic sinus. When aneurysms in this location do not rupture, signs of aortic insufficiency are absent. In a rare instance an aneurysm of the posterior aortic sinus may rupture into the left atrium and yield aortic insufficiency. Rarely an aneurysm of an aortic sinus may rupture into the left ventricle.

Rupture of an Acquired Aneurysm of the Ascending Aorta.—Under unusual circumstances an aneurysm of the ascending aorta developing on the basis of acquired disease may rupture into the pulmonary trunk or, less commonly, into the superior vena cava. Such an aneurysm may give a clinical picture of aortic insufficiency.

Traumatic "Incomplete" Rupture of the Aorta.—In patients being subjected to accidents involving sudden deceleration, the ascending aorta may rupture. In such instances the rupture may be through the entire thickness of the aorta, causing sudden death. When the rupture involves the

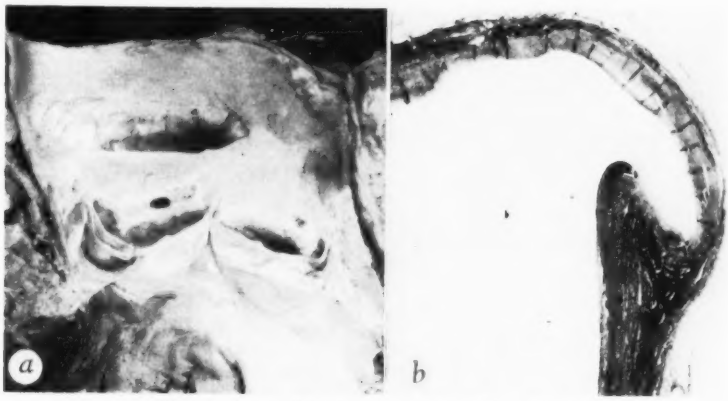


Fig. 9.—Incomplete rupture of ascending aorta.

(*a*) Aortic valve and portion of the ascending aorta. Above the aortic valve there is a defect in the wall of the aorta which represents incomplete rupture of the ascending aorta. The patient had been in a car accident 25 years before death. Though in this instance the incomplete rupture of the aorta did not cause aortic insufficiency, in some patients having somewhat similar lesions aortic insufficiency may exist.

(*b*) Longitudinal section of ascending aorta at the junction of intact vessel and area of incomplete rupture. In the lower right portion of the illustration the intact aortic wall suddenly loses its media, with the formation of an aneurysm. The aneurysm arches upward and to the left in the illustration. The intact aorta shows normal elastic layers, while in the aneurysm there are only remnants of aortic tissue present. Verhoeff's elastic tissue and Van Gieson's connective tissue stains; × 6.

aortic wall only incompletely, dilatation of the ascending aorta may occur (Fig. 9). The secondary effects of aortic dilatation on the aortic valve leaflets may be responsible for aortic insufficiency. Rarely deceleration accidents will be responsible for rupture of aortic valvular tissue, but it is commoner for the rupture, when present, to involve the aortic wall primarily.

Arteriovenous Communication Between a Coronary Artery and a Cardiac Chamber or the Coronary Sinus.—This is a rare example of a congenital communication between a coronary artery, on one hand, and the coronary sinus or any one of the four cardiac chambers, on the other. Such an abnormal communication is responsible for a run-off of the blood from the aorta and the functional effects of aortic insufficiency.

Marfan's Syndrome.—In patients having Marfan's syndrome (arachnodactyly) the aorta is congenitally weak. Dissecting aneurysm may occur, or the aorta may show uniform dilatation. In patients who have the latter phenomenon aortic insufficiency may be associated.[4] In this developmental syndrome the aortic insufficiency is probably brought about as a result of aortic dilatation comparable to the secondary effects on the aortic cusps in syphilitic aortitis.

Incompetence of the Mitral Valve

The Normal Mitral Valve (Fig. 10).—When mitral insufficiency is under consideration, it is appropriate first to review some of the aspects of the normal valve.[5,6] One of the two mitral leaflets is termed the "posterior (or lateral) leaflet," while the other is called the "anterior (aortic or medial) leaflet."

Often the basal attachment of each cusp is said to be the "mitral ring," and with this suggestion there is the implication that the two leaflets have similar structural relationships. This is a common error which must be corrected. The basal attachment of the posterior leaflet is to a strip of collagen, which for convenience may be termed the "ring," or "annulus." The ring also is attached to the endocardium of the left atrium and to the most superior aspect

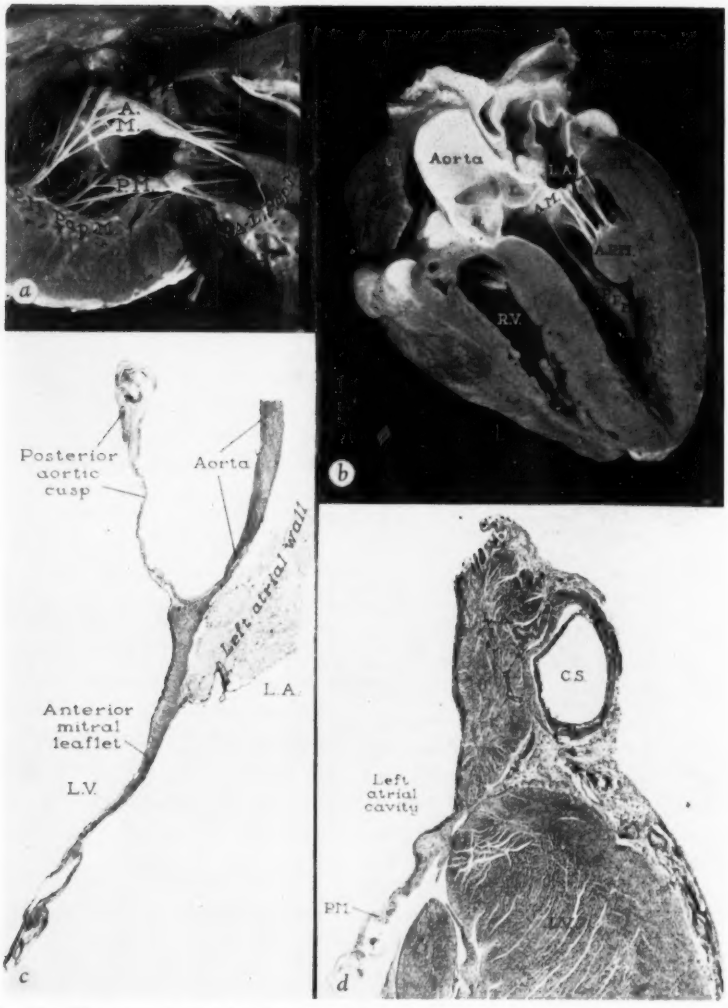


Fig. 10.—The normal mitral valve. (*a*) The mitral valve, which has been unopened, is viewed from the left ventricular aspect. The anterior mitral leaflet (*A. M.*) has chordal attachment to both the anterolateral (*A.-L.*) and the posteromedial (*P.-M.*) papillary muscles (*Pap. M.*). The posterior mitral leaflet (*P. M.*) has similar attachments. In view of the chordal attachment from each papillary muscle to each leaflet, one set of chordae may be viewed as having an effect opposing that of the other set.

(*b*) A longitudinal section through a normal heart. The plane of section lies just medial to the anterolateral commissure of the mitral valve. In this way the space between the anterior mitral (*A. M.*) and the posterior mitral (*P. M.*) leaflets represents the mitral orifice. Portrayed are the chordae which run from the anterolateral papillary muscle (*A. P. M.*) to each of the leaflets. Some of the chordae which run from the posteromedial papillary muscle (*P. P. M.*) to the leaflets at the region of the posteromedial commissure are also shown. The continuity of the aorta and aortic valve in the region of the posterior and adjacent left (*L.*) aortic leaflets with the anterior mitral leaflet is shown. The right aortic leaflet (*R.*) is distant from the mitral valve and closely related to the ventricular septum.

(*c*) A longitudinal section through the posterior aortic cusp, aorta, and anterior mitral leaflet. The plane of section is practically the same as in (*b*), but at a somewhat more posterior level. The level of the section shows in greater detail the anatomic relationships of the posterior aortic cusp. The adjacent part of the left aortic cusp has similar relationships, as illustrated in (*b*). The continuity of the aortic valvular tissue and the aortic wall with the anterior mitral leaflet is brought out. At this portion of the heart the aorta does not have direct connection with the myocardium but, instead, connects with the anterior mitral leaflet. Reproduced from article by Edwards and Burchell in the June, 1957, issue of *Thorax*, by permission of the British Medical Association.

(*d*) The posterior mitral leaflet. The endocardium of the left atrium is continuous with the posterior mitral leaflet. (*P. M.*) At the junction of these two structures union with the ventricular endocardium occurs also. At this region the annulus fibrosus is said to exist. (*C. S.* indicates coronary sinus.) The left atrial and left ventricular walls lie in about the same plane.

of the wall of the left ventricle. The relations at the ring are such that the posterior leaflet of the mitral valve is continuous with the endocardium of the left atrium (Fig. 10*b*). Any displacement of the left atrial endocardium will exert a pull on the posterior mitral leaflet.[7]

The anterior mitral leaflet, while also continuous with the left atrial endocardium, is more intimately connected with the aortic root and the adjacent portions of the left and posterior aortic cusps. At this area the origin of the aorta is joined only to mitral valvular tissue, whereas elsewhere the aortic root is joined to the myocardium of the left ventricle or ventricular septum.[8]

The junctional zones between the two mitral leaflets are the commissures, posteromedial and anterolateral. At each commissural region is a set of chordae tendineae, of which the upper attachments are to the particular commissural tissue and the adjacent parts of each leaflet. The lower attachment of a set of chordae is to a corresponding papillary muscle. Since each set of chordae makes attachment to each leaflet, one set of chordae may be said to be antagonistic to the other (Fig. 10*a*).

During ventricular diastole, when the normal mitral valve is open, the leaflets lie in vertical planes with respect to the long axis of the left ventricular cavity. During ventricular systole the two leaflets of the closed mitral valve lie in a plane at about right angles to the long axis of the left ventricle.

For the valve to open and close properly a number of factors must exist. These are (1) flexibility of the valvular tissue, (2) absence of undue fusion of one leaflet with the other at the commissures, (3) adequate effective length to the chordae, and (4) adequate length of the leaflets to make possible approximation of one with the other.

"Relative" Mitral Insufficiency.—The term "relative" mitral insufficiency is usually applied when the left ventricle is enlarged and the mitral valve seemingly is normal. A common teaching is that dilatation of the left ventricle causes dilatation of the ring, that is, enlargement of the mitral orifice. It is considered that this factor makes the mitral orifice so large that the normal leaflets cannot make contact. While such a factor may play a role, consideration should also be given to a chorda factor in the genesis of "relative" mitral insufficiency.

During ventricular contraction of the normal heart the mitral chordae are of such length as to allow the two leaflets to balloon upward and make contact.

In the presence of an enlarged left ventricular cavity the distance between the apices of the papillary muscles and the mitral orifice is probably greater than in the normal heart. Thus, for the same absolute movement of the papillary muscles toward the mitral orifice, the chordae would not allow the same upward movement of the leaflets as would occur with a normal-sized left ventricle. Thus a type of mitral insufficiency is possible in which normal leaflets are restrained from proper contact by the restraining influence of the chordae tendineae.

Rheumatic Mitral Insufficiency.—Theoretically, valvular disease causing incompetence of the mitral valve may result simply from intrinsic disease leading to shortening of the mitral leaflets. Practically, however, the process of mitral insufficiency is often more complicated. One factor, among others, is varying degrees of fusion of the two leaflets at one or both commissures. The existence of varying degrees of mitral stenosis often depends on the extent of this process of fusion. In some cases this feature may be the predominant one.

In this discussion, I should like to restrict the consideration to those cases in which the insufficiency is the significant lesion and in which the stenosis, although present in a strict structural sense, seems to contribute little to the functional disturbances.

Three significant changes cause insufficiency, but not all need contribute to mitral

insufficiency in a given heart. The changes are (1) calcification at the commissures holding the orifice open, (2) intrinsic shortening of the posterior mitral leaflet, and (3) relative shortening of the posterior mitral leaflet secondary to dilatation of the left atrium. These changes in varying combinations lead to more or less specific types of mitral insufficiency.

Chordal shortening may accentuate incompetence caused by valvular shortening.

Calcification at Both Commissures, Holding the Orifice Open: When calcification occurs at a commissure, it involves also the adjacent portions of the two mitral leaflets. In incompetent valves, at commissures so involved, the two leaflets are held open and fixed. Because of the valvular fixation,

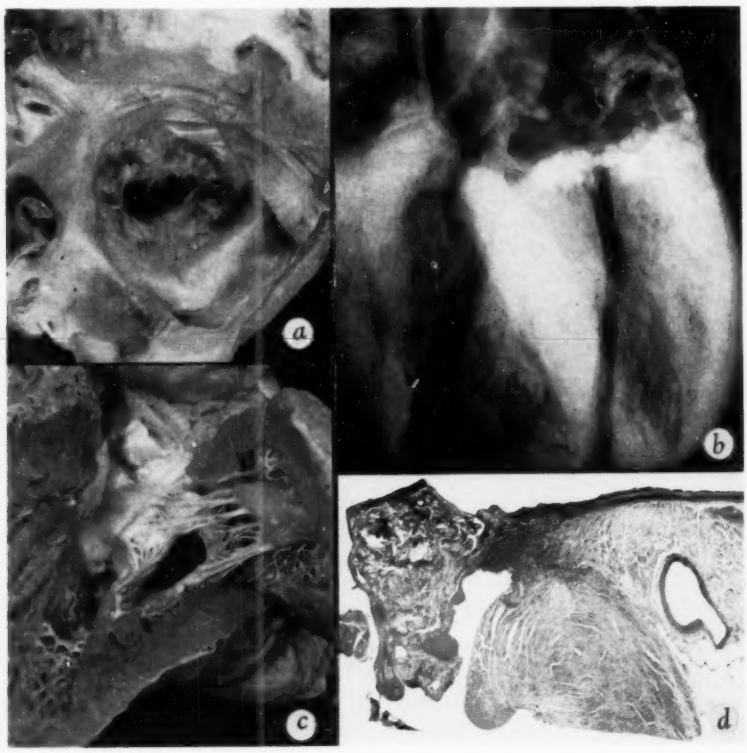
Fig. 11.—Rheumatic mitral insufficiency characterized by calcification at both commissures which hold the orifice open.

(*a*) The mitral orifice viewed from above. The anterior leaflet lies above, the posterior leaflet below. At each commissure there is calcification, which joins the two leaflets. Similar calcification in the valvular tissue, taken with the commissural fusion, creates a valve which is essentially an immobile structure and in which the orifice is open throughout the cardiac cycle.

(*b*) Roentgenogram of specimen of heart shown in (*a*) viewed from the side. Extreme calcification of the mitral valve may be noted.

(*c*) Mitral valve from the left ventricular aspect. Whereas the chordae are normal, the deficiency in closure of the orifice is brought about by fixation of the two leaflets in an open position, associated with some intrinsic shortening of the posterior leaflet. The latter structure is shown in the lower portion of the illustration.

(*d*) Left atrium, left ventricle, and posterior mitral leaflet showing the intrinsically shortened leaflet associated with marked calcification. The plane of the left atrial wall is at right angles to that of the left ventricular wall. Normally, these two lie in essentially the same plane. In spite of the distortion of the atrial wall, the posterior mitral leaflet has not been retracted, a feature prevented by the fusion of one leaflet to the other at each commissure. Verhoeff's elastic tissue and Van Gieson's connective tissue stains; reduced from mag. × 2.4.



incompetence exists regardless of the length of the valvular tissue, although often the valvular tissue is shortened (Fig. 11).

The calcification may involve both commissures. In the presence of this process the orifice is open and remains so through the entire extent of the valve.

Calcification at One Commissure with No Significant Involvement at the Other: Under these circumstances, the valve is held open in relation to the calcified focus. At the uninvolved commissure there is a theoretical possibility of partial closure of the valve by apposition of the two leaflets (Fig. 12).

Relative Shortening of Posterior Mitral Leaflet Due to Dilatation of the Atrium: Since the left atrial endocardium is continuous with the posterior leaflet of the mitral valve, tension is placed on this leaflet as the left atrium dilates. When the posterior leaflet is joined to the anterior leaflet by a process of commissural fusion, the posterior leaflet cannot be pulled away from the anterior one. It pulls the anterior leaflet with it, but this will not affect the orifice.

At a nonfused commissure, on the contrary, dilatation of the left atrium may pull the posterior leaflet away from the anterior one and create or accentuate incompetence, from intrinsic valvular shortening, at this region of the valve.

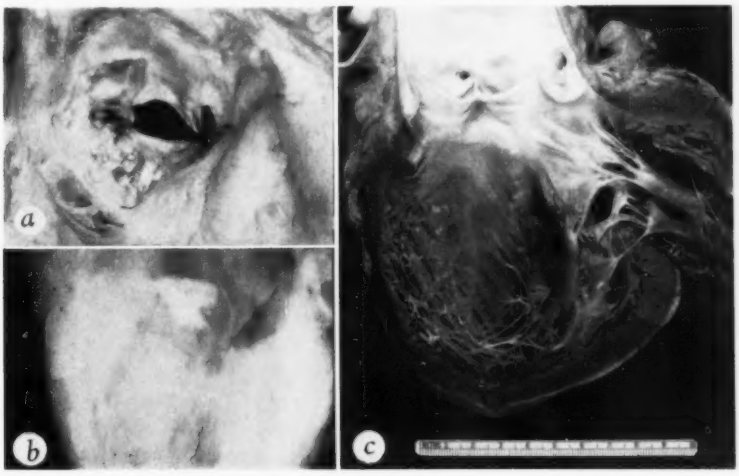
Commissural Fusion and Intrinsic Valvular Shortening: There may be moderate fusion at each commissure associated with valvular shortening. Commissural calcification may or may not be present. The incompetence results principally from intrinsic shortening of the posterior cusp (Fig. 13). It is important to recognize that the bicommissural fusion prevents left atrial dilatation from dislocating the posterior mitral leaflet posteriorly. This preventive function of commissural fusion is appreciated when in such a heart mitral

Fig. 12.—Rheumatic mitral insufficiency with fusion at one commissure.

(*a*) The mitral valve viewed from above. Fusion at the anterolateral commissure (left side of orifice from this view) holds the two leaflets in an open position at this portion of the valve. At the opposite end of the orifice, at the posteromedial commissure, fusion has not occurred. Retraction of the posterior leaflet in this area adds to the mitral insufficiency. Reproduced from article by Burchell and Edwards in the May, 1953, issue of *Circulation* page 747, by permission of the publishers, Grune & Stratton, Inc.

(*b*) Deposit of calcium in the anterolateral commissure and in adjacent valvular tissue. Roentgenogram made from specimen.

(*c*) Left ventricle. The mitral valve is viewed from below. The anterolateral commissure lies to the right side of the orifice in this perspective. The valve is held open by calcification at the commissure. Shortening of the leaflet due in part to intrinsic disease and in part to retraction resulting from the dilatation of the left atrium is present.



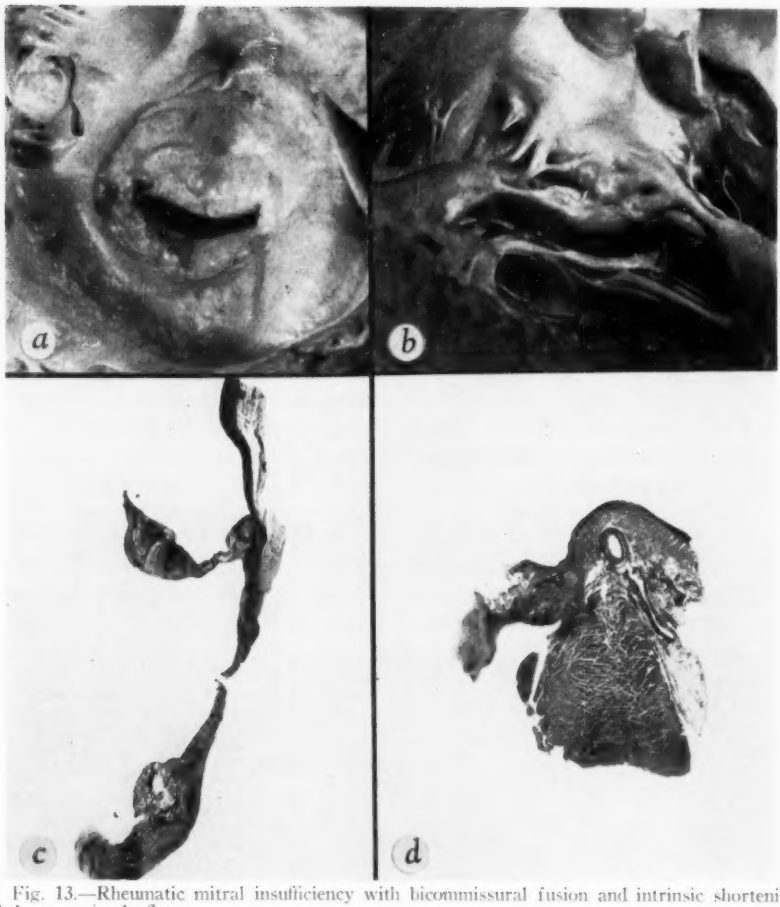


Fig. 13.—Rheumatic mitral insufficiency with bicommissural fusion and intrinsic shortening of the posterior leaflet.

(*a*) Mitral valve viewed from above. There is mild fusion at each commissure. The valve is incompetent, mainly on the basis of shortening of the posterior leaflet.

(*b*) Mitral valve viewed from the left ventricular aspect, showing relatively little involvement of chordae but considerable intrinsic shortening of the posterior leaflet.

(*c*) Left aortic leaflet and anterior mitral leaflet. There is fibrous and focal calcific thickening of both the aortic leaflet and the anterior mitral leaflet. In spite of the involvement of the anterior mitral leaflet, the amount of shortening is relatively small as compared with the changes in the posterior leaflet, which are illustrated in (*d*). Verhoeff's elastic tissue stain, counterstained with Van Gieson's connective tissue stain; × 2.5.

(d) Left atrium, left ventricle, and posterior mitral leaflet. There is considerable intrinsic shortening of the posterior leaflet. Although the left atrium shows histologic evidence of dilatation, with a change in plane of its wall, the annulus fibrosus has not been displaced. This is accounted for by the fact that at each commissure there was fusion which prevented the process of dislocation of the posterior leaflet. Verhoeff's elastic tissue stain, counterstained with Van Gieson's connective tissue stain; × 2.5.

commissurotomy is followed by accentuation of the degree of mitral insufficiency.

Other Forms of Mitral Insufficiency.—It is not my intention to discuss in detail forms of mitral insufficiency other than those of rheumatic origin. These have been presented in an earlier communication.[9]

It is proper, however, to point out one feature.

Rheumatic mitral insufficiency, even when it is the only significant abnormality, is usually associated with some degree of

mitral stenosis. However minor the latter is, it may be identified by appropriate pressure studies of the left atrium and ventricle.

When such studies fail to reveal at least some hemodynamic evidence of mitral obstruction in a case of mitral insufficiency, the physician has justification for considering less common types of mitral insufficiency than those of rheumatic origin. Included among these are rupture of mitral chordae, healed bacterial endocarditis, and various types of congenital mitral insufficiency.

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Infarction of an Accessory Lobe of the Liver

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Accessory lobes of the liver are noted infrequently at necropsy or as an incidental finding at the time of abdominal surgery. These lobes rarely give rise to conditions requiring surgical intervention. Accessory lobes of the liver are small and may be attached to the liver by a mesentery or liver parenchyma. These lobes are generally attached to the undersurface of the liver and are noted on the right more frequently than on the left. Accessory lobes have been noted arising separately from the gall bladder and gastrohepatic ligament and in the suspensory ligament.[2]

Only two previous cases could be found in the literature in which an accessory lobe of the liver produced manifestations demanding surgical intervention.[1,3] Fraser [3] reported an accessory lobe of the liver, 12 cm. in diameter, presenting as a palpable abdominal mass. Exploration was required to determine the true etiology of the mass. Cullen,[1] in 1925, reported the only instance of torsion of the mesentery to an accessory lobe of the liver, producing infarction and manifesting signs of acute abdominal disease. A second such case will be presented.

Report of a Case

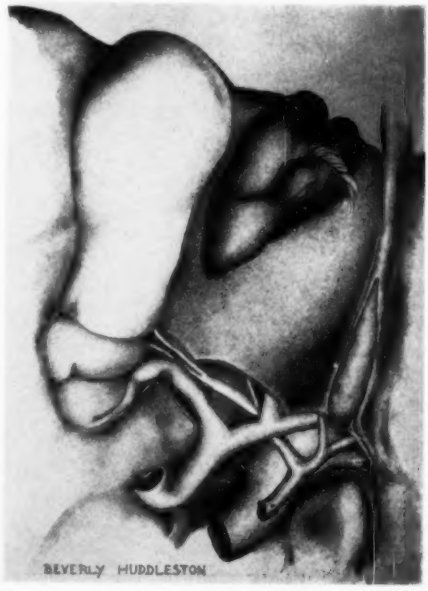
A 19-year-old Negro youth was admitted to the Confederate Memorial Medical Center with the complaint of abdominal pain of four days' duration. The pain was cramping in nature, originated in the periumbilical area, and radiated into the right upper quadrant of the abdomen. Vomiting of a greenish watery material occurred twice on the day of admission. The review of systems was noncontributory. Appendectomy had been performed four years prior to admission.

Physical Examination.—The patient was a muscular young Negro, who appeared acutely ill. He was afebrile. The positive findings were limited to the abdomen, where there was noted generalized abdominal tenderness to palpation. Muscle guarding and rebound tenderness were present, and moderate, in the right upper quadrant. Bowel sounds were not audible.

Laboratory Data.—The total white cell count was 7200 per cubic millimeter, with 78 segmented and 2 stab-form neutrophils and 20 lymphocytes. Hemoglobin was 14.7 gm. %. Urinalysis was normal. A sickle-cell preparation was normal. Flat and erect films of the abdomen showed moderately dilated loops of small bowel in the midabdomen, without demonstrable fluid levels.

Hospital Course.—Constant nasogastric suction was instituted and intravenous fluid therapy begun. The patient was observed over a 14-hour period, during which the abdominal findings became more pronounced. Abdominal exploration was then performed, revealing omentum closely adherent to a small triangular (3×6×4 cm.), reddish-black mass. The mass was connected to the undersurface of

An artist's sketch of the accessory lobe of the liver, showing torsion of its mesentery and its relationship to the gallbladder and liver.



Submitted for publication April 1, 1958.

From the Department of Surgery, Confederate Memorial Medical Center.

the right lobe of the liver by a 2 cm. mesentery. This mesentery had undergone torsion of 360 degrees. The infarcted accessory lobe of the liver was removed simply by dividing its mesentery. The patient made an uneventful recovery.

Pathological Report.—"There is evidence of liver tissue in the section, characterized by the appearance of blood in a cord-like arrangement, blood vessels that appear to be in a peripheral location, and an outer rim of capsule; otherwise, features are distorted by infarction in such a manner that the architecture is no longer present."

Summary

A case of infarction of an accessory lobe of the liver due to torsion of its mesentery is presented. This case showed signs and symptoms of acute abdominal disease, which required surgical intervention. This is the second such case to be reported.

Confederate Memorial Medical Center, Kings Highway at Linwood.

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The Autoplastic Cutis Vascular Graft

Report of Cases

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Successful surgical treatment of obliterative arterial disease, as well an aneurysm, has been established. However, the modus operandi is still in a state of flux, insofar as the replacement material to be employed is concerned. De Bakey,[1] who has published the greatest series of cases to date, has given up the use of the homograft in most instances and is now employing a crimped Dacron prosthesis. Shumacker[2] and Edwards[3] have been utilizing the crimped nylon tube wherever feasible.

It is certainly understandable and logical that employment of these materials has sparked the advances and dramatic results in the amelioration of symptoms, as well as cure, of those unfortunate patients with occlusive arterial disease, as has Sputnik in the missiles race.

However, in those communities where the vascular bank is nonexistent, or the vascular bank is wanting, or the "stockpile" of synthetic prostheses is not present, or the "size" is not in stock, what would one use in any catastrophic situation, whether it be an inadvertent surgical accident, or an immediate surgical requirement in the operating room, or in the military, where the necessity for immediate definitive vascular replacement presents itself? It is with the foregoing question in mind, that we present the following material. We have had the opportunity to apply the autoplastic cutis vascular graft in three cases, after several years' observation in our experimental animals. The results and histologic studies have been recorded in two previous communications.[4,5] After considering the histological architecture of the applied graft and noting that it is a "live tissue" (Figure), we felt that it warranted human application.

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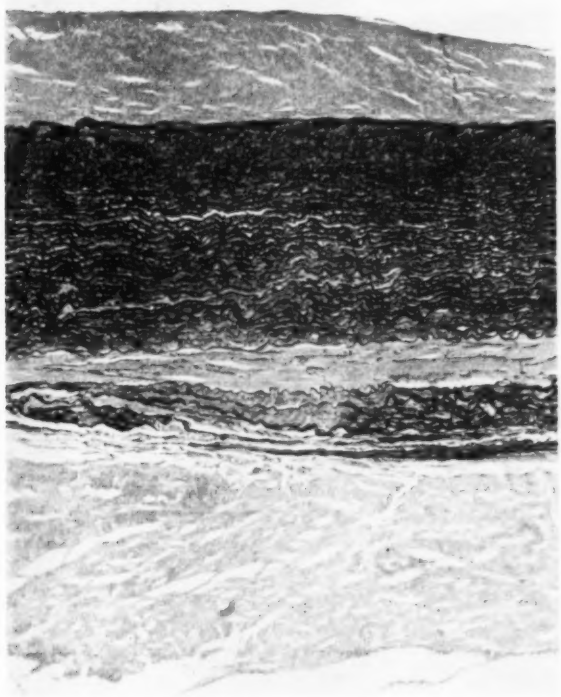
Supported by Grant-in-Aid from the American Heart Association, Inc.

From the Departments of Anatomy, Surgery, and Pathology, Marquette University School of Medicine.

Associate, Department of Anatomy; Clinical Instructor in Surgery (Dr. Wagner). Associate Professor, Department of Anatomy (Dr. Benjamin). Professor and Chief of Department of Anatomy (Dr. Zeit). Professor and Chief of Department of Pathology (Dr. Kuzma).

Surgical Procedure in Preparation of the Graft

Under general anesthesia, the patient was prepared in the usual manner from the xyphoid process to the knees. With the Brown dermatome, a skin graft was taken 0.025 inch thick, 3 in. wide, and 9 in. long. This graft was discarded, and "the shaved" segment of skin was undercut, including the superficial subcutaneous tissue. This cutis graft was placed in saline until ready for use. The autoplastic skin vascular graft was tailored in the following manner: The diameter of the femoral artery was measured with calipers, and a glass mandrel of the same diameter was employed. The rod was glycerinized, and the "shaved" dermal side of the skin graft was heparinized, placed about the mandrel, and sutured with a Lembert stitch, employing 0000 silk; a second line of suture approximate the edges of the subcutaneous layer of the graft. When the tube was tested, it was leakproof, and, the graft having been tailored to the exact size was applied as a bypass implant, as was needed. The skin defect in the



High-power photomicrograph of a six-month skin prosthesis stained especially for elastic tissue, showing a wide "intimal" connective tissue cushion. Elastic fibers are parallel and are concentrated in the inner half of the thickness. The adventitial layer manifests no apparent host reaction.

abdominal wall, the site where the cutis graft was taken, was closed by a Z-plasty procedure.

CASE 1.—A 43-year-old white man was first seen in January, 1957, with the chief complaint of pain in his left leg. He stated that if he walked half a block he would experience pain in the calf of his leg. His past medical history was essentially negative save for the fact that he had sustained a fracture of the left ankle five years prior to the date of examination. The pain in his calf was aggravated with cold, and the intermittent claudication had become progressively worse, so that he was barely able to walk half a block. He also began to experience pain during the night, so that he would have to get out of bed, shake his leg, or take a little walk to relieve it.

Pertinent findings in the patient's work-up revealed that he had no femoral pulse on the left side, and no oscillometric thrust on the left, either above or below the knee. The temperature of the left lower extremity was approximately 2 degrees (F) below that of the right. The patient was hospitalized, and aortography revealed an occlusion of the common iliac artery. A bypass procedure was performed from the aorta to the femoral artery, employing the cutis vascular graft, with gratifying results. This patient has pursued his work with no apparent difficulty, having been checked in September, 1957. He had a return of pulsation of the ankle vessels.

CASE 2.—A 51-year-old white man had suffered coronary thrombosis in November, 1956. He was seen in February, 1957, because of pain in his calf and foot after prolonged standing or walking two blocks. Examination revealed no pulsation of the popliteal or ankle vessels; oscillometry showed only one digit thrust below the knee on the right leg, as compared with a six-digit thrust on the left leg. This man had intermittent claudication, as noted above, and arteriography revealed occlusion of the superficial femoral artery at the distal segment of Hunter's canal. A bypass procedure was accomplished from the proximal segment of the superficial femoral artery to the popliteal artery, employing the cutis vascular graft. The patient had an uneventful recovery, with return of ankle-vessel pulsations. The patient was last examined on Dec. 23, 1957; he was asymptomatic, could walk four to five blocks with no apparent claudication, and worked a full eight hours as a cabinet worker. The patient made his own observation three months after surgery that he had return of growth of hair on his great toe.

CASE 3.—A 62-year-old white man, a brewery worker, presented the chief complaint of pain in the right leg of approximately three years' duration. He experienced intermittent claudication with walking or dancing. Physical examination revealed no femoral pulsation on the right side, with no oscillometric thrust above the knee on the right, as compared with a six-digit thrust on the left. Aortography revealed occlusion of the common iliac artery on the right. The patient was taken to surgery in April, 1957, and a bypass procedure was performed from the aorta to the femoral artery, using the cutis vascular graft. The patient had an uneventful recovery. After operation, he had return of pulsation in the ankle vessels. Two weeks after operation the patient was able to ascend stairs and walk eight blocks with no apparent difficulty. The patient was last examined Dec. 6, 1957; he was asymptomatic and was back to work.

Comment

Although we may be presumptuous in reporting these three cases, the oldest graft having been applied only 11 months, we feel that our application of this type of graft satisfies the primary requirements of a vascular prosthesis; i. e., (1) it is autogenous, (2) it can be "tailored" to the exact size at the operating table, and (3) every person is his own vascular bank. The other very important consideration we find from our histologic studies is that the cutis grafts applied are "live" tissue, as was noted in the Figure. Certainly, we concede the argument of "why fuss and bother making a graft" if we have on the "shelf" a synthetic stockpile of "goods" (nylon or Dacron) from which we may draw as necessary; however, it is in those instances, in which such a supply is lacking, as we have noted in our preface to this paper, that we feel our autoplastic cutis vascular prosthesis can play an important role, if it is not used as an elective material for vascular replacement or bypass.

Summary

Three cases are presented; three autoplastic cutis vascular grafts have been applied. The advantages of this graft are outlined, as well as their purpose and location of use.

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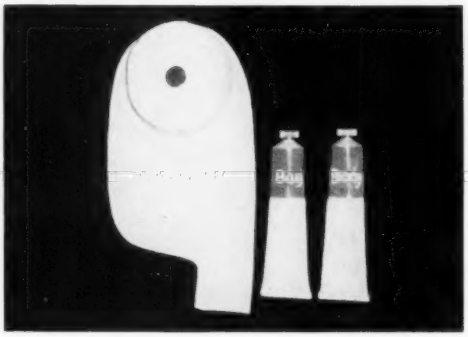

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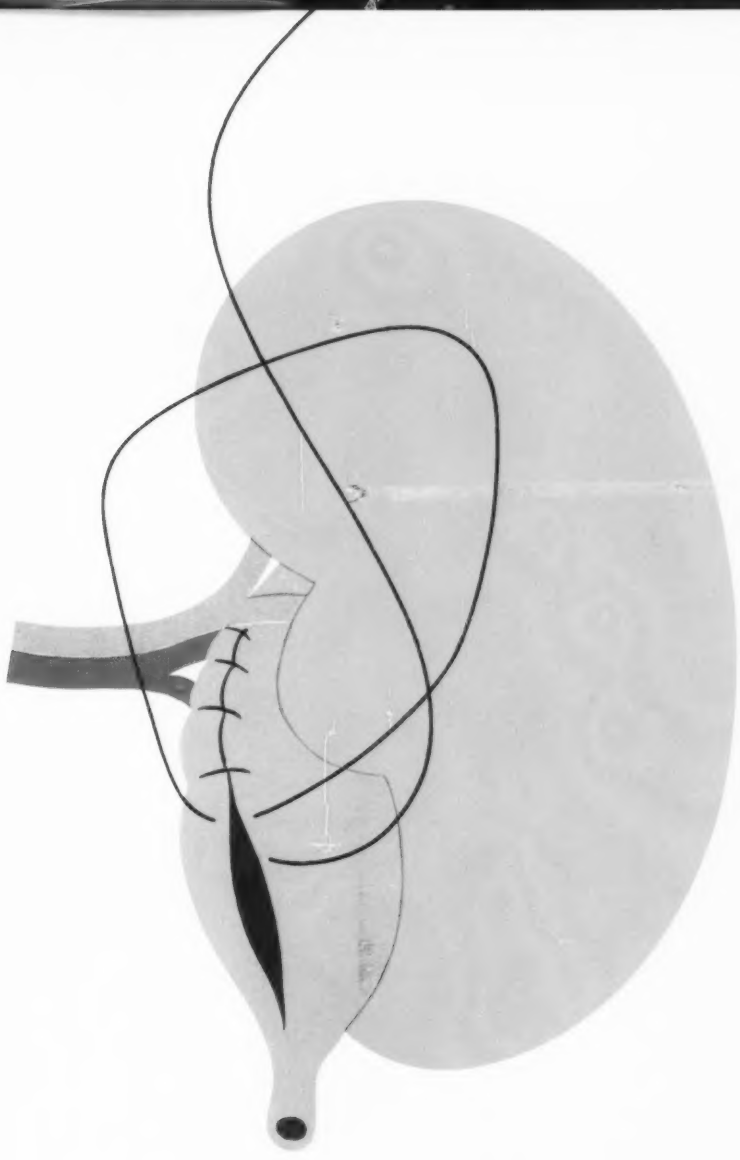

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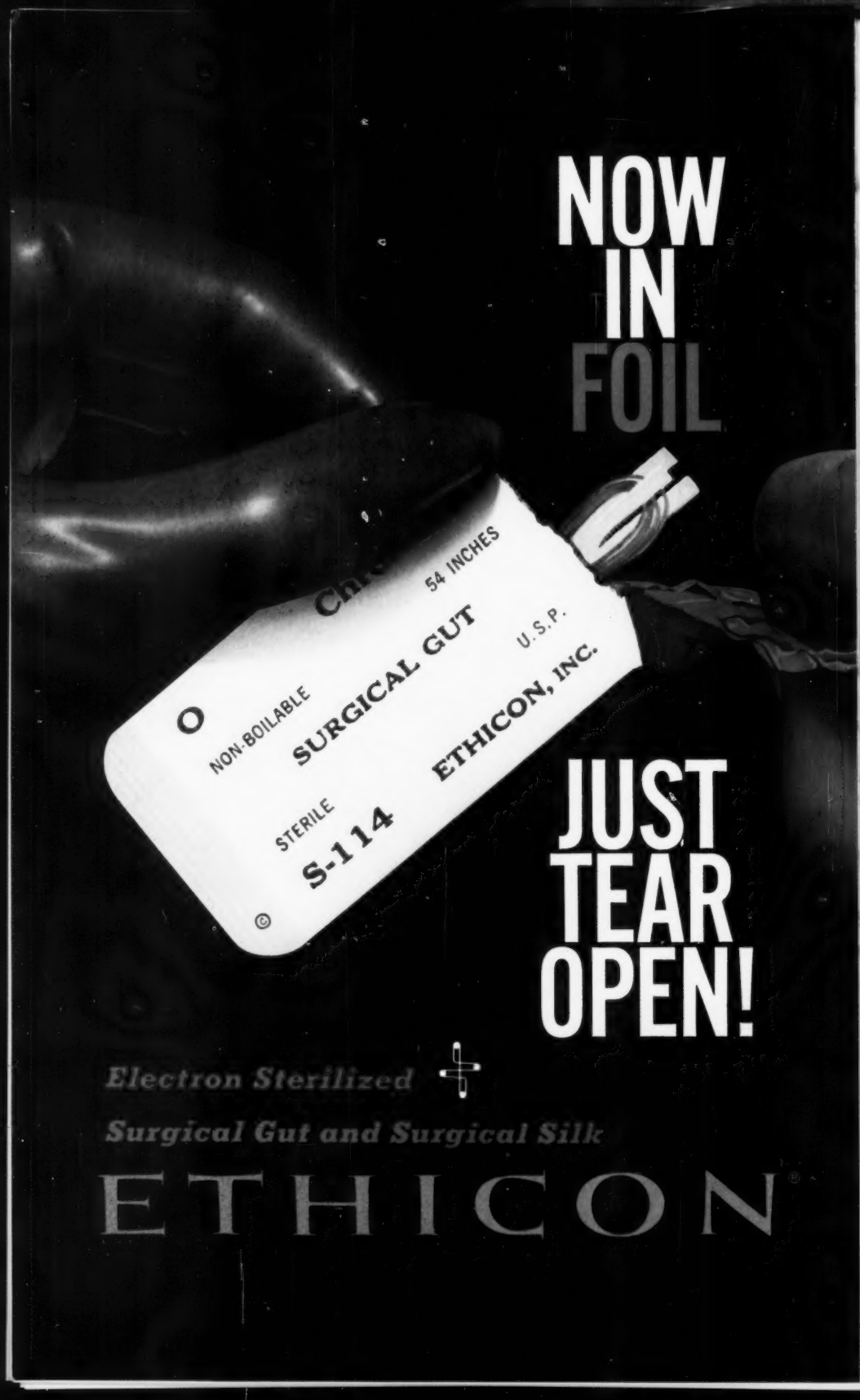
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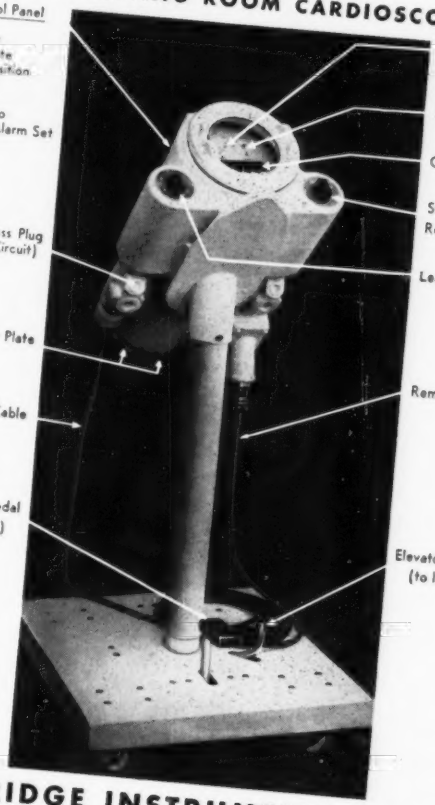

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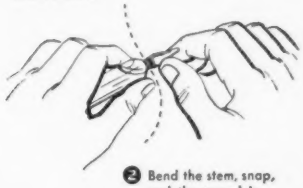

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